WHO Coronavirus (COVID-19) Dashboard

Date Filed: 10/06/2022 Page: 1 of 95
Overview Measures Table View Data M

More Resources



Document: 44-2

Globally, as of 4:59pm CEST, 4 October 2022, there have been 615,777,700 confirmed cases of COVID-19, including 6,527,192 deaths, reported to WHO. As of 28 September 2022, a total of 12,677,499,928 vaccine doses have been administered.



Morbidity and Mortality Weekly Report (MMWR)

Weekly / May 27, 2022 / 71(21);713-717

On May 24, 2022, this report was posted online as an MMWR Early Release.

Lara Bull-Otterson, PhD¹; Sarah Baca¹,²; Sharon Saydah, PhD¹; Tegan K. Boehmer, PhD¹; Stacey Adjei, MPH¹; Simone Gray, PhD¹; Aaron M. Harris, MD¹ (VIEW AUTHOR AFFILIATIONS)

View suggested citation

Summary

What is already known about this topic?

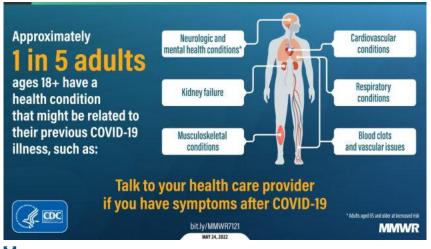
As more persons are exposed to and infected by SARS-CoV-2, reports of patients who experience persistent symptoms or organ dysfunction after acute COVID-19 and develop post-COVID conditions have increased.

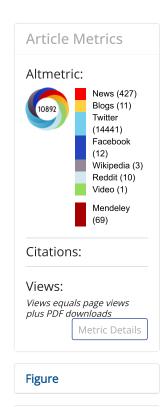
What is added by this report?

COVID-19 survivors have twice the risk for developing pulmonary embolism or respiratory conditions; one in five COVID-19 survivors aged 18–64 years and one in four survivors aged ≥65 years experienced at least one incident condition that might be attributable to previous COVID-19.

What are the implications for public health practice?

Implementation of COVID-19 prevention strategies, as well as routine assessment for post-COVID conditions among persons who survive COVID-19, is critical to reducing the incidence and impact of post-COVID conditions, particularly among adults aged ≥65 years.





Table

References

PDF 🔼 [121K]

Related Materials

View Larger

A growing number of persons previously infected with SARS-CoV-2, the virus that causes COVID-19, have reported persistent symptoms, or the onset of long-term symptoms, \geq 4 weeks after acute COVID-19; these symptoms are commonly referred to as post-COVID conditions, or long COVID (1). Electronic health record (EHR) data during March 2020–November 2021, for persons in the United States aged \geq 18 years were used to assess the incidence of 26 conditions often attributable to post-COVID (hereafter also referred to as incident conditions) among patients who had received a previous COVID-19 diagnosis (case-patients) compared with the incidence among matched patients without evidence of COVID-19 in the EHR (control

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 3 of 95 patients). The analysis was stratified by two age groups (persons aged 18-64 and ≥65 years). Patients were followed for 30-

365 days after the index encounter until one or more incident conditions were observed or through October 31, 2021 (whichever occurred first). Among all patients aged ≥18 years, 38% of case-patients experienced an incident condition compared with 16% of controls; conditions affected multiple systems, and included cardiovascular, pulmonary, hematologic, renal, endocrine, gastrointestinal, musculoskeletal, neurologic, and psychiatric signs and symptoms. By age group, the highest risk ratios (RRs) were for acute pulmonary embolism (RR = 2.1 and 2.2 among persons aged 18–64 and ≥65 years, respectively) and respiratory signs and symptoms (RR = 2.1 in both age groups). Among those aged 18–64 years, 35.4% of case-patients experienced an incident condition compared with 14.6% of controls. Among those aged ≥65 years, 45.4% of case-patients experienced an incident condition compared with 18.5% of controls. These findings translate to one in five COVID-19 survivors aged 18–64 years, and one in four survivors aged ≥65 years experiencing an incident condition that might be attributable to previous COVID-19. Implementation of COVID-19 prevention strategies, as well as routine assessment for post-COVID conditions among persons who survive COVID-19, is critical to reducing the incidence and impact of post-COVID, particularly among adults aged ≥65 years (2).

A retrospective matched cohort design was used to analyze EHRs during March 2020–November 2021, from Cerner Real-World Data,* a national, deidentified data set of approximately 63.4 million unique adult records from 110 data contributors in the 50 states. Case-patients (353,164) were adults aged ≥18 years who received either a diagnosis of COVID-19 or a positive SARS-CoV-2 test result⁺ (case-patient index encounter) in an inpatient, emergency department, or outpatient settings within a subset of health care facilities that use Cerner EHRs. Control patients (1,640,776) had a visit in the same month as the matched case-patient (control index encounter) and did not receive a COVID-19 diagnosis or a positive SARS-CoV-2 test result during the observation period. Controls were matched 5:1 with case-patients. All patients included in the analysis were required to have at least one encounter in their EHR during the year preceding and the year after the index encounter.

The occurrence of 26 clinical conditions previously attributed to post-COVID illness was assessed by review of the scientific literature (3-5) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/117411). Patients were followed for 30–365 days after the index encounter until the first occurrence of an incident condition or until October 31, 2021, whichever occurred first. Case-patients or control patients with a previous history of one of the included conditions in the year before the index encounter were excluded (478,072 patients). The analysis was stratified by age into two groups: adults aged 18–64 and adults aged \geq 65 years. Incidence rates per 100 person-months, and RRs with 95% CIs, were calculated. The number of COVID-19 case-patients having experienced an incident condition was also estimated by age group. Nonoverlapping CIs between age groups were considered statistically significant. Analyses were performed using RStudio Workbench (version 3.0; RStudio). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.**

Among all patients aged \geq 18 years, 38.2% of case-patients and 16.0% of controls experienced at least one incident condition (Table). Among persons aged 18–64 years, 35.4% of case-patients and 14.6% of controls experienced at least one incident condition. Among persons aged \geq 65 years, 45.4% of case-patients and 18.5% of controls experienced at least one incident condition. The absolute risk difference between the percentage of case-patients and controls who developed an incident condition was 20.8 percentage points for those aged 18–64 years and 26.9 percentage points for those aged \geq 65 years. This finding translates to one in five COVID-19 survivors aged 18–64 years and one in four survivors aged \geq 65 years experiencing an incident condition that might be attributable to previous COVID-19.

The most common incident conditions in both age groups were respiratory symptoms and musculoskeletal pain (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/117411). Among both age groups, the highest RRs were for incident conditions involving the pulmonary system, including acute pulmonary embolism (RR = 2.2 [patients aged \geq 65 years] and 2.1 [patients aged 18–64 years]) and respiratory symptoms (RR = 2.1, both age groups) (Figure). Among patients aged \geq 65 years, the risks were higher among case-patients than among controls for all 26 incident conditions, with RRs ranging from 1.2 (substance-related disorder) to 2.2 (acute pulmonary embolism). Among patients aged 18–64 years, the risks were higher among case-patients than among controls for 22 incident conditions, with RRs ranging from 1.1 (anxiety) to 2.1 (acute pulmonary embolism); no significant difference was observed for cerebrovascular disease, or mental health conditions, such as mood disorders, other mental conditions, and substance-related disorders.

Differences by age group were noted. The RR for cardiac dysrhythmia was significantly higher among patients aged 18–64 years (RR = 1.7) compared with those aged \geq 65 years (1.5). Similarly, the RR for musculoskeletal pain was higher among patients aged 18–64 years (1.6) than among those aged \geq 65 years (1.4). Among case-patients, the RRs for 10 incident conditions was significantly higher among those aged \geq 65 years than among those aged 18–64 years; these conditions were renal failure, thromboembolic events, cerebrovascular disease, type 2 diabetes, muscle disorders, neurologic conditions, and mental health conditions (including mood disorders, anxiety, other mental conditions, and substance-related disorders).

The findings from this analysis of a large EHR-based database of U.S. adults indicated that COVID-19 survivors were significantly more likely than were control patients to have incident conditions that might be attributable to previous COVID-19. One in five COVID-19 survivors aged 18–64 years and one in four survivors aged ≥65 years experienced at least one incident condition that might be attributable to previous COVID-19. Independent of age group, the highest RRs were for acute pulmonary embolism and respiratory symptoms.

These findings are consistent with those from several large studies that indicated that post-COVID incident conditions occur in 20%-30% of patients (6,7), and that a proportion of patients require expanded follow-up care after the initial infection. COVID-19 severity and illness duration can affect patients' health care needs and economic well-being (8). The occurrence of incident conditions following infection might also affect a patient's ability to contribute to the workforce and might have economic consequences for survivors and their dependents, particularly among adults aged 18-64 years (5). In addition, care requirements might place a strain on health services after acute illness in communities that experience heavy COVID-19 case surges.

COVID-19 survivors aged \geq 65 years in this study were at increased risk for neurologic conditions, as well as for four of five mental health conditions (mood disorders, other mental conditions, anxiety, and substance-related disorders). Neurocognitive symptoms have been reported to persist for up to 1 year after acute infection and might persist longer (*9*). Overall, 45.4% of survivors aged \geq 65 years in this study had incident conditions. Among adults aged \geq 65 years, who are already at higher risk for stroke and neurocognitive impairment, post-COVID conditions affecting the nervous system are of particular concern because these conditions can lead to early entry into supportive services or investment of additional resources into care (*10*).

The findings in this study are subject to at least five limitations. First, patient data were limited to those seen at facilities serviced by Cerner EHR network during January 2020-November 2021; therefore, the findings might not be representative of the entire U.S. adult population or of COVID-19 case patients infected with recent variants. Second, the incidence of new conditions after an acute COVID-19 infection might be biased toward a population that is seeking care, either as a follow-up to a previous complaint (including COVID-19) or for another medical complaint, which might result in a "sicker" control group leading to underestimation of observed risk. Third, COVID-19 vaccination status was not considered in this analysis, nor were potentially confounding factors (e.g., SARS-CoV-2 variant, sex, race, ethnicity, health care entity, or geographic region), because data were not available, were inconsistent, or included a high proportion of missing or unknown values; for example, data were not matched by data contributors, so controls were not necessarily from the same health care entity or region of the country. Differences between the groups might influence the risks associated with survival from COVID-19 and incident conditions, which require further study. Fourth, International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) codes were used to identify COVID-19 case-patients, and misclassification of controls is possible. However, the inclusion of laboratory data to identify case-patients and exclude controls helped to limit the potential for such misclassification. Finally, the study only assessed conditions thought to be attributable to COVID-19 or post-COVID illness, which might have biased RRs away from the null. For example, clinicians might have been more likely to document possible post-COVID conditions among case-patients. In addition, because several conditions examined are also risk factors for moderate to severe COVID-19, it is possible that case-patients were more likely to have had an existing condition that was not documented in their EHR during the year preceding their COVID-19 diagnosis, resulting in overestimated risk for this group.

As the cumulative number of persons ever having been infected with SARS-CoV-2 increases, the number of survivors suffering post-COVID conditions is also likely to increase. Therefore, implementation of COVID-19 prevention strategies, as well as routine assessment for post-COVID conditions among persons who survive COVID-19, is critical to reducing the incidence and impact of post-COVID conditions, particularly among adults aged ≥65 years (2). These findings can increase awareness for post-COVID conditions and improve post-acute care and management of patients after illness. Further investigation is warranted to understand the pathophysiologic mechanisms associated with increased risk for post-COVID conditions, including by age and type of condition.

Corresponding author: Lara Bull-Otterson, lbull@cdc.gov

Top

Top

Top

- * https://www.cerner.com/solutions/real-world-data? ga=2.134259058.2081252678.1649198012-1806687702.1649105445
- [†] COVID-19 cases with associated positive test result were identified by the following: Systematized Nomenclature of Medicine (SNOMED) codes 840533007, 840535000, 840539006, and 840546002; *International Classification of Diseases, Tenth Edition, Clinical Modification* (ICD-10-CM) codes B97.29 (March, 2020) and U07.1 (April–May 2020); and Logical Observation Identifiers Names and Codes (LOINC) codes 68993–5, 92142–9, 92141–1, 94309–2, 94307–6, 94308–4, 94500–6, 94502–2, 94533–7, 94534–5, 94559–2, 94756–4, 94757–2, 94758–0, 94845–5, 95406–5, 95409–9, 96091–4, 95425–5, 95423–0, and 96448–6.
- § Acute myocardial infarction, cardiac dysrhythmias, cardiovascular disease, heart failure, myocarditis and cardiomyopathy, acute pulmonary embolism, respiratory symptoms, asthma, renal failure, chronic kidney disease, thromboembolic event, cerebrovascular disease, coagulation and hemorrhagic conditions, gastrointestinal and esophageal conditions, neurologic conditions, smell and taste disturbances, mood disorders, other mental conditions, anxiety and fear-related conditions, sleeping disorders, substance-related disorders, malaise and fatigue, muscle disorders, musculoskeletal pain, diabetes type 2, and diabetes type 1.
- ¶ Calculated as the reciprocal of the absolute risk difference of COVID-19 case-patients and non–COVID-19 controls that experience at least one incident condition.
- ** 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Top

References

- 1. CDC. Long COVID or post-COVID conditions. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed April 22, 2022. https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html
- 2. Antonelli M, Penfold RS, Merino J, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. Lancet Infect Dis 2022;22:43-55. https://doi.org/10.1016/S1473-3099(21)00460-6 PMID:34480857
- 3. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. Nature 2021;594:259–64. https://doi.org/10.1093/cid/ciab338 2 PMID:33909072 2
- 4. Cohen K, Ren S, Heath K, et al. Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study. BMJ 2022;376:e068414. https://doi.org/10.1136/bmj-2021-068414 PMID:35140117
- 5. Rajan S, Khunti K, Alwan N, et al. In the wake of the pandemic: preparing for long COVID. Copenhagen, Denmark: European Observatory on Health Systems and Policies; 2021. PMID:33877759
- 7. Donnelly JP, Wang XQ, Iwashyna TJ, Prescott HC. Readmission and death after initial hospital discharge among patients with COVID-19 in a large multihospital system. JAMA 2021;325:304–6. https://doi.org/10.1001/jama.2020.21465 PMID:33315057
- 8. CDC. Science brief: indicators for monitoring COVID-19 community levels and making public health recommendations. Atlanta, GA: US Department of Health and Human Services; 2022. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/indicators-monitoring-community-levels.html
- 10. Mohamed MS, Johansson A, Jonsson J, Schiöth HB. Dissecting the molecular mechanisms surrounding post-COVID-19 syndrome and neurological features. Int J Mol Sci 2022;23:4275. https://doi.org/10.3390/ijms23084275 ☐ PMID:35457093 ☐

Top

USC	A11 Case	: 21-1272	9 Docur	ment: 44-2	Date Filed:	10/06/2022 Page: 6 of 95	
Ago	No. of patients (column %)		No. of patients with ≥1 incident condition (column %*)				
Age group, yrs	Case- patients	Control patients	Case- patients	Control patients	Absolute risk difference [†]	No. of COVID-19 survivors with a post-COVID condition [§]	
18-64	254,345 (72.0)	1,051,588 (64.1)	90,111 (35.4)	154,011 (14.6)	20.8	1/5	
≥65	98,819 (28.0)	589,188 (35.9)	44,840 (45.4)	108,850 (18.5)	26.9	1/4	
Total	353,164 (100)	1,640,776 (100)	134,951 (38.2)	262,861 (16.0)	22.2	1/4–5	

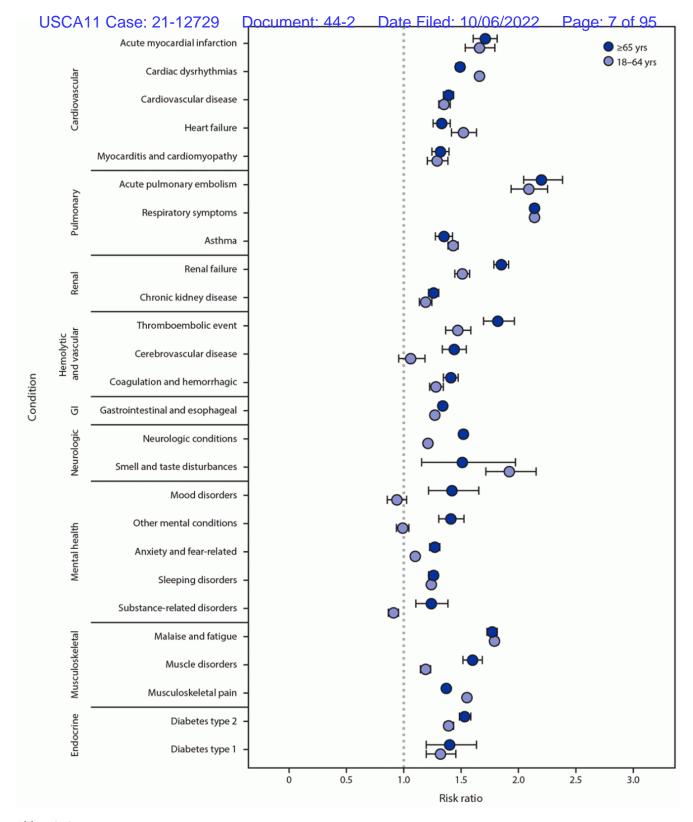
^{*} Percentage of COVID-19 case-patients or control patients with ≥1 incident condition divided by the total study COVID-19 cohort or control cohort row's age group total.

FIGURE. Risk ratios* for devēloping post-COVID conditions among adults agēd 18–64 years and ≥65 years — Unitēd States, March 2020– November 2021



[†] Percentage point difference between COVID-19 case-patients and control patients (e.g., the value 20.8 is calculated as 35.4 minus 14.6).

[§] Number of COVID-19 survivors who experienced a post-COVID condition estimated as the inverse of the absolute risk difference.



Abbreviation: GI = gastrointestinal.

Top

^{*} With CIs indicated by error bars; some error bars are not visible because of small CIs.

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 8 of 95

MMWR and Morbidity and Mortality Weekly Report are service marks of the U.S. Department of Health and Human Services.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of pages found at these sites. URL addresses listed in *MMWR* were current as of the date of publication.

All HTML versions of *MMWR* articles are generated from final proofs through an automated process. This conversion might result in character translation or format errors in the HTML version. Users are referred to the electronic PDF version (https://www.cdc.gov/mmwr) and/or the original *MMWR* paper copy for printable versions of official text, figures, and tables.

Questions or messages regarding errors in formatting should be addressed to $\label{eq:cdc.gov.} mmwrq@cdc.gov.$

Page last reviewed: May 26, 2022





COVID-19

Long COVID or Post-COVID Conditions

Updated Sept. 1, 2022

DEFINITION

Post-COVID Conditions

Some people who have been infected with the virus that causes COVID-19 can experience long-term effects from their infection, known as post-COVID conditions (PCC) or long COVID.

People call post-COVID conditions by many names, including: long COVID, long-haul COVID, post-acute COVID-19, post-acute sequelae of SARS CoV-2 infection (PASC), long-term effects of COVID, and chronic COVID.

What You Need to Know

- Post-COVID conditions can include a wide range of ongoing health problems; these conditions can last weeks, months, or longer.
- Post-COVID conditions are found more often in people who had severe COVID-19 illness, but anyone who has been infected with the virus that causes COVID-19 can experience post-COVID conditions, even people who had mild illness or no symptoms from COVID-19.
- People who are not vaccinated against COVID-19 and become infected might also be at higher risk of developing post-COVID conditions compared to people who were vaccinated and had breakthrough infections.
- While most people with post-COVID conditions have evidence of infection or COVID-19 illness, in some cases, a person with post-COVID conditions may not have tested positive for the virus or known they were infected.
- CDC and partners are working to understand more about who experiences post-COVID conditions and why, including whether groups disproportionately impacted by COVID-19 are at higher risk.

As of July 2021, "long COVID," also known as post-COVID conditions, can be considered a disability under the Americans with Disabilities Act (ADA). Learn more: Guidance on "Long COVID" as a Disability Under the ADA, Section 🖸

About Long COVID or Post-COVID Conditions

Post-COVID conditions are a wide range of new, returning, or ongoing health problems that people experience after being infected with the virus that causes COVID-19. Most people with COVID-19 get better within a few days to a few weeks after infection, so at least four weeks after infection is the start of when post-COVID conditions could first be identified. Anyone who was infected can experience post-COVID conditions. Most people with post-COVID conditions experienced symptoms days after first learning they had COVID-19, but some people who later experienced post-COVID conditions did not know when they got infected.

There is no test to diagnose post-COVID conditions, and people may have a wide variety of symptoms that could come from other health problems. This can make it difficult for healthcare providers to recognize post-COVID conditions. Your healthcare provider considers a diagnosis of post-COVID conditions based on your health history, including if you had a diagnosis of

Science at CDC

Scientific evidence and studies behind long COVID

Science behind Long COVID

How to Get Involved in Long COVID Research

The National Institutes of Health (NIH) is conducting a research project, called the RECOVER Initiative, to understand how people recover from a COVID-19 infection and why some people do not fully recover and develop long COVID or post-COVID conditions.

RECOVER: Researching COVID to Enhance Recovery ☑

Symptoms

People with post-COVID conditions (or long COVID) may experience many symptoms.

People with post-COVID conditions can have a wide range of symptoms that can last more than four weeks or even months after infection. Sometimes the symptoms can even go away or come back again.

Post-COVID conditions may not affect everyone the same way. People with post-COVID conditions may experience health problems from different types and combinations of symptoms happening over different lengths of time. Most patients' symptoms slowly improve with time. However, for some people, post-COVID conditions can last weeks, months, or longer after COVID-19 illness and can sometimes result in disability.

People who experience post-COVID conditions most commonly report:

General symptoms

- · Tiredness or fatigue that interferes with daily life
- Symptoms that get worse after physical or mental effort (also known as "post-exertional malaise")
- Fever

Respiratory and heart symptoms

- Difficulty breathing or shortness of breath
- Cough
- Chest pain
- Fast-beating or pounding heart (also known as heart palpitations)

Neurological symptoms

- Difficulty thinking or concentrating (sometimes referred to as "brain fog")
- Headache
- Sleep problems
- Dizziness when you stand up (lightheadedness)
- Pins-and-needles feelings
- Change in smell or taste
- Depression or anxiety

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 11 of 95

Stomach pain

Other symptoms

- Joint or muscle pain
- Rash
- Changes in menstrual cycles

Symptoms that are hard to explain and manage

Some people with post-COVID conditions have symptoms that are not explained by tests.

People with post-COVID conditions may develop or continue to have symptoms that are hard to explain and manage. Clinical evaluations and results of routine blood tests, chest x-rays, and electrocardiograms may be normal. The symptoms are similar to those reported by people with ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) and other poorly understood chronic illnesses that may occur after other infections. People with these unexplained symptoms may be misunderstood by their healthcare providers, which can result in a long time for them to get a diagnosis and receive appropriate care or treatment. Review these tips to help prepare for a healthcare provider appointment for post-COVID conditions.

Health conditions

Some people experience new health conditions after COVID-19 illness.

Some people, especially those who had severe COVID-19, experience multiorgan effects or autoimmune conditions with symptoms lasting weeks or months after COVID-19 illness. Multiorgan effects can involve many body systems, including the heart, lung, kidney, skin, and brain. As a result of these effects, people who have had COVID-19 may be more likely to develop new health conditions such as diabetes, heart conditions, or neurological conditions compared with people who have not had COVID-19.

People experiencing any severe illness may develop health problems

People experiencing any severe illness, hospitalization, or treatment may develop problems such as post-intensive care syndrome, or PICS.

PICS refers to the health effects that may begin when a person is in an intensive care unit (ICU), and which may persist after a person returns home. These effects can include muscle weakness, problems with thinking and judgment, and symptoms of post-traumatic stress disorder (PTSD). PTSD involves long-term reactions to a very stressful event. For people who experience PICS following a COVID-19 diagnosis, it is difficult to determine whether these health problems are caused by a severe illness, the virus itself, or a combination of both.

People More Likely to Develop Long COVID

Some people may be more at risk for developing post-COVID conditions (or long COVID).

Researchers are working to understand which people or groups of people are more likely to have post-COVID conditions, and why. Studies have shown that some groups of people may be affected more by post-COVID conditions. These are examples and not a comprehensive list of people or groups who might be more at risk than other groups for developing post-COVID conditions:

- People who have experienced more severe COVID-19 illness, especially those who were hospitalized of needed intensive care.
- People who had underlying health conditions prior to COVID-19.
- People who did not get a COVID-19 vaccine.
- People who experience multisystem inflammatory syndrome (MIS) during or after COVID-19 illness.

Health Inequities May Affect Populations at Risk for Long COVID

Some people are at increased risk of getting sick from COVID-19 because of where they live or work, or because they can't get health care. Health inequities may put some people from racial or ethnic minority groups and some people with disabilities at greater risk for developing post-COVID conditions. Scientists are researching some of those factors that may place these communities at higher risk of both getting infected or developing post-COVID conditions.

Preventing Long COVID

The best way to prevent post-COVID conditions is to protect yourself and others from becoming infected. For people who are eligible, getting vaccinated and staying up to date with vaccines against COVID-19 can help prevent COVID-19 infection and protect against severe illness.

Research suggests that people who are vaccinated but experience a breakthrough infection are less likely to report post-COVID conditions, compared to people who are unvaccinated.

Learn more about protecting yourself and others from COVID-19.

Living with Long COVID

Living with a post-COVID condition can be hard, especially when there are no immediate answers or solutions.

However, people experiencing post-COVID conditions can seek care from a healthcare provider to come up with a personal medical management plan that can help improve their symptoms and quality of life. Review these tips to help prepare for a healthcare provider appointment for post-COVID conditions. In addition, there are many support groups being organized that can help patients and their caregivers.

Although post-COVID conditions appear to be less common in children and adolescents than in adults, long-term effects after COVID-19 do occur in children and adolescents.

Calk to your doctor if you think you or your child has long COVID or a post-COVID condition. Learn more: Tips for Talking to Your Healthcare Provider about Post-COVID Conditions

Data for Long COVID

Studies are in progress to better understand post-COVID conditions and how many people experience them.

CDC is using multiple approaches to estimate how many people experience post-COVID conditions. Each approach can provide a piece of the puzzle to give us a better picture of who is experiencing post-COVID conditions. For example, some studies look for the presence of post-COVID conditions based on self-reported symptoms, while others collect symptoms and conditions recorded in medical records. Some studies focus only on people who have been hospitalized, while others include people who were not hospitalized. The estimates for how many people experience post-COVID conditions can be quite different depending on who was included in the study, as well as how and when the study collected information. Estimates of the proportion of people who had COVID-19 that go on to experience post-COVID conditions can vary:

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 13 of 95

- 2.5% at three months or longer, based on self-reporting
- More than 30% at 6 months among patients who were hospitalized

CDC and other federal agencies, as well as academic institutions and research organizations, are working to learn more about the short- and long-term health effects associated with COVID-19 \(\mathbb{C}\), who gets them and why.

Scientists are also learning more about how new variants could potentially affect post-COVID symptoms. We are still learning to what extent certain groups are at higher risk, and if different groups of people tend to experience different types of post-COVID conditions. These studies, including for example CDC's INSPIRE and NIH's RECOVER . will help us better understand post-COVID conditions and how healthcare providers can treat or support patients with these longer-term effects. CDC will continue to share information with healthcare providers to help them evaluate and manage these conditions. CDC is working to:

- Better identify the most frequent symptoms and diagnoses experienced by patients with post-COVID conditions.
- Better understand how many people are affected by post-COVID conditions, and how often people who are infected with COVID-19 develop post-COVID conditions afterwards.
- Better understand risk factors, including which groups might be more at risk, and if different groups experience different symptoms.
- Help understand how post-COVID conditions limit or restrict people's daily activity.
- Help identify groups that have been more affected by post-COVID conditions, lack access to care and treatment for post-COVID conditions, or experience stigma.
- Better understand the role vaccination plays in preventing post-COVID conditions.
- Collaborate with professional medical groups to develop and offer clinical guidance and other educational materials for healthcare providers, patients, and the public.

Related Pages

- Caring for People with Post-COVID Conditions
- > Preparing for Appointments for Post-COVID Conditions
- ➤ Researching COVID to Enhance Recovery
- > Guidance on "Long COVID" as a Disability Under the ADA ☐

For Healthcare Professionals

> Post-COVID Conditions: Healthcare Providers

Last Updated Sept. 1, 2022

Latest information on COVID-19

News Center



Search News...

0

News / Story

Brain fog after COVID-19 has similarities to 'chemo brain,' Stanford-led study finds

share **f y** ir

Researchers found that damage to the brain's white matter after COVID-19 resembles that seen after cancer chemotherapy, raising hope for treatments to help both conditions.

June 13, 2022 - By Erin Digitale

Brain fog after COVID-19 is biologically similar to cognitive impairment caused by cancer chemotherapy, something doctors often refer to as "chemo brain." In both cases, excessive inflammation damages the same brain cells and processes, according to research led by Stanford University School of Medicine.

The discovery, described in a paper that published online June 12 in *Cell*, relied on studies of mice with mild SARS-CoV-2 infection and postmortem human brain tissue collected early in the pandemic. The findings may help guide treatments for cognitive effects of COVID-19, the scientists said.



"We found that even mild COVID can cause prominent inflammation in the brain that dysregulates brain cells and would be expected to contribute to cognitive impairment," said Michelle Monje, MD, PhD, professor of neurology and neurological sciences.

Researchers at Stanford Medicine have found biological similarities between "chemo brain" — cognitive impairment from cancer treatment — and brain fog after COVID-19.

Jolygon/Shutterstock.com

Monje shares senior authorship of the study with

Akiko Iwasaki, PhD, professor of immunology and of molecular, cellular and developmental biology at Yale University. The study's lead authors are Anthony Fernandez-Castaneda, PhD, a postdoctoral scholar at Stanford; Anna Geraghty, PhD, an instructor of neurology at Stanford; and Peiwen Lu, PhD, and graduate student Eric Song, both of Yale.

The overlap between what happens in COVID-19's cognitive aftermath and chemo brain, as it's colloquially known, could be good news for patients because it may speed research on treatments, Monje said. "The exciting message is that because the pathophysiology is so similar, the last couple of decades in cancer therapy-related research can guide us to treatments that may help COVID brain fog."

Nerves' insulation damaged

Monje's team has spent two decades studying cognitive impairment after cancer. They uncovered key details in how chemotherapy impairs the function of the brain's white matter, regions of the brain normally rich in well-insulated nerve fibers that quickly transmit signals from one place to another. Myelin, the fatty coating insulating the long arms of the neurons, helps speed the transmission of nerve signals. In chemo brain, damage to myelin slows their transmission.

"When the pandemic started, I started worrying that we would see similar neurological consequences of this profoundly immunogenic virus," Monje said. Because the virus caused such a strong immune response, including widespread inflammation, she suspected it might also cause cognitive problems.

Many COVID-19 survivors experience cognitive impairment. Stanford research published in March 2021, covering the first year of the pandemic, found that about one in four COVID-19 patients had cognitive symptoms that lingered at least two months, even after mild infections. Patients' symptoms included impairments to attention, concentration, memory and executive function, as well as slower information processing — all of which are also common among people who experience chemo brain after cancer treatment.

Monje and her colleagues examined brain changes in mice in which the researchers had induced SARS-CoV-2 infections confined to the respiratory system. Mice lack the cellular receptors that the SARS-CoV-2 virus uses to invade human cells, but animals in the study were genetically engineered to express the necessary receptors in the respiratory tract. After exposure to SARS-CoV-2, the mice had mild infections: They did not lose weight or behave as though they were ill, and the virus was not found in their brains.



Michelle Monje

Nevertheless, scientists saw more of several inflammatory cytokines in the blood and cerebrospinal fluid of the mice, increases that could be detected one and seven weeks after infection. In their white matter, the microglia — brain cells that support neurons and "eat" cellular debris in the brain — were much more active than normal, an abnormality that persisted seven weeks after infection.

After mild COVID-19, analysis of gene activity in single cells uncovered more microglia with high levels of pro-inflammatory molecules called chemokines and more activity in genes involved in inflammation. The genes expressed in microglia after COVID-19 overlapped closely with those expressed by microglia in other disease contexts, including cognitive decline in aging and in neurological conditions such as Alzheimer's disease. This finding lines up with prior work linking microglial reactivity to poor cognitive function.

Microglial reactivity was particularly high in the hippocampus, a brain center involved in learning and memory. The researchers found that one of the elevated chemokines called CCL11 can directly cause microglial reactivity specifically in the hippocampus. The formation of new neurons in the hippocampus of the mice was impaired, likely due to the cytokine changes and the increased reactivity of microglia.

After infection, the mice also showed changes among cells in the white matter that help coat the neurons in insulating myelin. The cells that create myelin, called oligodendrocytes, were harmed by mild COVID-19, with the number of mature oligodendrocytes and cells destined to be oligodendrocytes declining in the brains of mice following SARS-CoV-2 infection. The researchers also found a loss of myelin, evident as a decrease in the density of myelinated axons in the white matter, which could be detected by one week and persisted seven weeks after infection.

Because other viral infections can cause brain inflammation, the researchers studied brain changes in mice after mild respiratory infection with H1N1 influenza, the viral strain that caused the 2009 "swine flu" and 1918 "Spanish flu" pandemics. The goal was to compare cognition-linked molecular changes after H1N1 to those seen after COVID-19. One week after infection, the H1N1 flu and SARS-CoV-2 infections caused similar patterns of cytokine elevation in the central nervous system, microglial reactivity and loss of oligodendrocytes in white matter. But seven weeks after infection, although the cytokine profiles had some overlap, including increased inflammatory chemokine CCL11, they differed. Effects on the hippocampus were similar in the two types of infections, but microglial reactivity and oligodendrocyte loss in white matter were not present after seven weeks following H1N1 infection.

The shorter-lasting and less-severe brain changes seen in mice after H1N1 infection are consistent with less prevalent reports of cognitive symptoms after this type of infection, highlighting that respiratory infections can change the brain even if the virus does not infect the brain, the researchers said.

Human data similar to animal findings

To further confirm their findings, the researchers examined data from brain tissue collected from a small group of people who had died suddenly in New York City in the spring of 2020. The human brain tissue came from five people who died with incidental SARS-CoV-2 infection (meaning they died for reasons that may have been unrelated to COVID-19, such as accidents); four people who died with known COVID-19 symptoms, including two who had been hospitalized in intensive care; and nine people in the control group who died without SARS-CoV-2 infection. People with SARS-CoV-2 infection were examined for lung injury and were not found to have had the most severe form of pneumonia. These people had no evidence of brain infection. However, those with COVID-19 had greater microglial reactivity than those in the control group, in a pattern that matched what was found in the mice.

In another group of 48 people who developed long COVID-19 with cognitive symptoms, the inflammatory cytokine CCL11 blood levels were elevated compared with those of 15 long- COVID patients who did not have cognitive symptoms.

Monje's team is already conducting research on medications that could alleviate brain fog after chemotherapy, and they plan to investigate whether these drugs are helpful after SARS-CoV-2 infection.

"While there are many similarities to cognitive impairment after cancer, there are probably differences, too," she said. "We need to test any potential therapies explicitly for COVID."

Monje is a member of Stanford Bio-X, the Stanford Institute for Stem Cell Biology and Regenerative Medicine, Stanford's Maternal and Child Health Research Institute, the Stanford Cancer Institute, and the Stanford Wu Tsai Neurosciences Institute.

Scientists from Yale University, the National Institute of Neurological Disorders and Stroke, the Mount Sinai School of Medicine, New York University Grossman School of Medicine, the National Cancer Institute, the Uniformed Services University of Health Sciences, University of Iowa, the Office of the Chief Medical Examiner (New York City), and the Howard Hughes Medical Institute (at Yale and at Stanford) also contributed to the research.

The research was supported by the National Institute of Neurological Disorders and Stroke (grants R01NS092597, NS003130 and NS003157), the National Institute of Allergy and Infectious Diseases (grant R01AI157488), an NIH Director's Pioneer Award (DP1NS111132), the Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation, Cancer Research UK, the Waxman Family Research Fund, Fast Grant for Emergent Ventures at the Mercatus Center, and the Howard Hughes Medical Institute.



Erin Digitale is the pediatrics science writer in the Office of Communications. Email her at digitale@stanford.edu.

Media Contacts
Erin Digitale
Tel 650-724-9175
digitale@stanford.edu

Stanford Medicine integrates research, medical education and health care at its three institutions - Stanford School of Medicine, Stanford Health Care, and Stanford Children's Health. For more information, please visit the Office of Communications website at http://mednews.stanford.edu.

₩ Find People

Q Visit Stanford

✓ Search Clinical Trials

Give a Gift

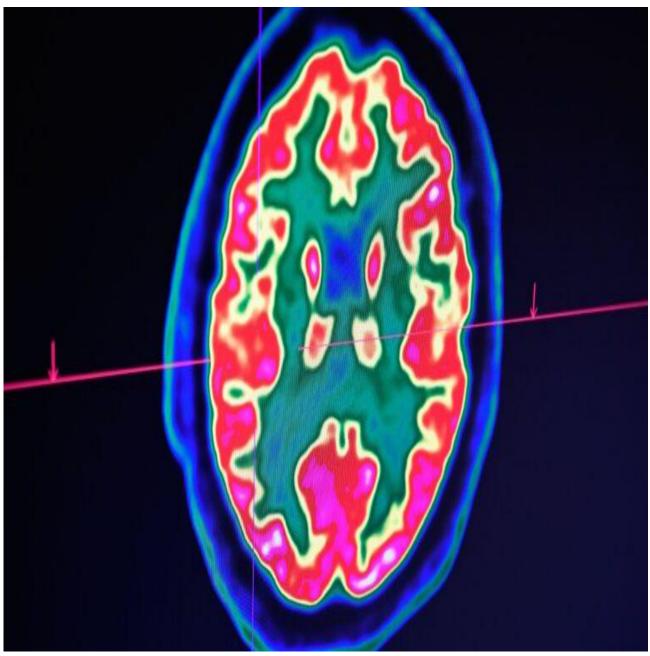
©2022 Stanford Medicine

STAT

Risk of 'brain fog' and other conditions persists up to two years after Covid infection



By Elizabeth Cooney Aug. 17, 2022



PET scan of a brain FRED TANNEAU/AFP via Getty Images

Among the many worrying consequences of Covid-19, neuropsychiatric conditions rank high. A <u>year ago</u> researchers from Oxford University reported that 1 in 3 patients experienced mood disorders, strokes, or dementia six months after Covid infection. Now the same group is back with a longer-term analysis of 1.25 million Covid patient records, including what they believe is the first large-scale look at children and at new variants.

Their news is both bad and good.

Up to two years after Covid-19 infection, the risk of developing conditions such as psychosis, dementia, "brain fog," and seizures is still higher than after other respiratory infections, the researchers report in their <u>study</u> published Wednesday in the Lancet Psychiatry. But while anxiety and depression are more common soon after a Covid-19 diagnosis, the mood disorders are transient, becoming no more likely after the two months than following similar infections such as flu.

Children were not more likely to be diagnosed with anxiety or depression, right away or up to two years after Covid, and their risk of brain fog subsided over two years. But they were still more likely than children recovering from other respiratory infections to have seizures and psychotic disorders. Overall, the likelihood of all these diagnoses was lower in children than in adults.

On variants, the risk of neuropsychiatric diagnoses rose, from 10% higher for anxiety to 38% for brain fog — after the Delta variant emerged than after the alpha version. Similar risks continued with Omicron, even though that variant has milder effects during the acute phase of infection.

"What these data show in this very large cohort retrospectively analyzed is that the mood disorders and anxiety problems that are really, really prevalent in long Covid tended to resolve in a matter of months, which is great news for patients with long Covid who are not used to suffering in those ways," Wes Ely, a critical care physician at Vanderbilt University Medical Center and associate director for research for the VA Tennessee Valley Geriatric Research and Education Clinical Center, told STAT. He was not involved in the Oxford studies.

"The other finding of this fascinating investigation is that the cognitive problems, the neurocognitive deficits that make people have brain fog, do not resolve so quickly," he said. "Clinically, in my own practice and in our long Covid clinic, this is exactly what we're seeing: that the acquired dementia that these patients get tends to be lasting and very problematic."

To reach their conclusions, the Oxford team combed through data on 14 neurological and psychiatric diagnoses entered into electronic health records in the TriNetX network, mostly from the U.S., over a two-year period. For a control group, the 1.25 million Covid patients were matched with an equal number of patients with any other respiratory infection and no history of Covid. Compared with the people in the control group:

- Adults under 65 with a history of Covid infection up to two years previously had a higher risk of cognitive deficit, better known as brain fog (640 vs. 550 cases per 10,000 people), and muscle disease (44 vs. 32 cases per 10,000 people).
- Adults 65 and over who had Covid over the same time span had more diagnoses of brain fog (1,540 vs. 1,230 per 10,000 people), dementia (450 vs. 330 per 10,000 people), and psychotic disorder (85 vs. 60 per 10,000 people).
- Children who had Covid were more likely to have seizures (260 vs. 130 cases per 10,000 children) and psychotic disorders (18 vs. 6 per 10,000 children).

Max Taquet, National Institute for Health and Care Research academic clinical fellow in psychiatry at Oxford and a study co-author, stressed that the elevated risk for seizures and psychotic disorders in children was still

low. "It's important to keep in mind the absolute numbers are often very small, much smaller than in adults," he said on a call with reporters.

Taquet made the same point about adults. "I think it's very clear that this is not a tsunami of new dementia cases," he said. "Equally, I think it's hard to ignore it, given the severity of the consequences of dementia diagnoses. A 1.2% increase in the population in absolute terms and compared to in other previous infections is hard to ignore."

Paul Harrison, professor of psychiatry at Oxford and a study co-author, said these numbers were still important. "Certainly for some conditions, there appears to be a nontrivial and persisting greater risk of these diagnoses being made," he said on the call with reporters. "And for some of those diagnoses, it's highly likely that those people are going to need medical attention."

While waiting for the mechanisms of long Covid — and any potential treatments — to be understood, "What's important for me as a physician is that we know that we can have long-term outcomes in very severe persistent and disabling, neuropsychiatric disorders," some of which can be treated, Teodor Postolache, professor of psychiatry at the University of Maryland School of Medicine, said.

An editorial published with the paper sounds a note of caution on psychiatric diagnoses.

"Dementia has an insidious onset, and the cohort is likely to have had some participants with undiagnosed or subclinical cases at baseline," Jonathan Rogers and Glyn Lewis of University College London write. "Although concerning, the findings regarding psychosis and dementia need replication in a cohort in which there is more thorough ascertainment of case status."

Electronic health records have limitations in how well they reveal complicated neuropsychiatric conditions — which might mean they are underreported, another long Covid researcher said. "I can tell you for a fact that it is really difficult to express in medical records, particularly if you're busy doing a lot of them, all the nuances that sort of go along with the neurocognitive issues," Steven Deeks, a professor of medicine at University of California, San Francisco, told STAT. "This stuff can be subtle. This is only picking up very blunt stuff. At the end of the day, it provides additional proof that long Covid is real, that some people can have profound symptoms, and that they can persist for a couple of years."

Rachel Sumner, a senior research fellow at Cardiff Metropolitan University, called the study results "alarming" while Covid continues to spread. "The finding of complex and potentially severe psychiatric and neurological fallout of Covid infection adds yet more weight and concern to the impact of repeated infections that will occur should the virus continue to be allowed to spread to re-infect with little to no control," she said in a statement.

The study didn't explore the causes of the neuropsychiatric illnesses, but Vanderbilt's Ely said the prevalence it reports lines up with emerging research on different parts of the brain being affected by the SARS-CoV-2 virus, corresponding to mood disorders and to cognitive impairment. And he's worried about what comes next.

"This paper ... fits the narrative both of clinically what I see in practice, but also the actual brain science that we're coming up against," he said. As for cognitive impairment, he said, "This is something that is very hard for people to cope with because they can't go back to work. They have to retire early, and they desperately need answers."

About the Author



Elizabeth Cooney

Reporter, Morning Rounds Writer

Liz is the author of STAT's Morning Rounds newsletter.

elizabeth.cooney@statnews.com
@cooney_liz
2 Comments

Create a display name to comment

This name will appear with your comment





Research

Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission

David N. Fisman, Afia Amoako and Ashleigh R. Tuite CMAJ April 25, 2022 194 (16) E573-E580; DOI: https://doi.org/10.1503/cmaj.212105

Article	Figures & Tables	Related Content	Responses
Metrics	₽DF		

Abstract

Background: The speed of vaccine development has been a singular achievement during the COVID-19 pandemic, although uptake has not been universal. Vaccine opponents often frame their opposition in terms of the rights of the unvaccinated. We sought to explore the impact of mixing of vaccinated and unvaccinated populations on risk of SARS-CoV-2 infection among vaccinated people.

Methods: We constructed a simple susceptible–infectious–recovered compartmental model of a respiratory infectious disease with 2 connected subpopulations: people who were vaccinated and those who were unvaccinated. We simulated a spectrum of patterns of mixing between vaccinated and unvaccinated groups that ranged from random mixing to complete like-with-like mixing (complete assortativity), in which people have contact

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue Find out more

Results: We found that the risk of infection was markedly higher among unvaccinated people than among vaccinated people under all mixing assumptions. The contact-adjusted contribution of unvaccinated people to infection risk was disproportionate, with unvaccinated people contributing to infections among those who were vaccinated at a rate higher than would have been expected based on contact numbers alone. We found that as likewith-like mixing increased, attack rates among vaccinated people decreased from 15% to 10% (and increased from 62% to 79% among unvaccinated people), but the contact-adjusted contribution to risk among vaccinated people derived from contact with unvaccinated people increased.

Interpretation: Although risk associated with avoiding vaccination during a virulent pandemic accrues chiefly to people who are unvaccinated, their choices affect risk of viral infection among those who are vaccinated in a manner that is disproportionate to the portion of unvaccinated people in the population.

The remarkable speed of vaccine development, production and administration during the COVID-19 pandemic is a singular human achievement. While the ability to vaccinate to herd immunity has been held back by the increasing transmissibility of novel SARS-CoV-2 variants of concern (e.g., Delta and Omicron variants), and global distribution of vaccines is inequitable, the effectiveness of SARS-CoV-2 vaccines in reducing severity of disease and disrupting onward transmission even when breakthrough infections occur is likely to have saved many lives. The emergence of the immune-evasive Omicron variant may undermine some of these gains, although provision of booster vaccine doses may restore vaccination to a high level of potency, and vaccines developed specifically to enhance immunity to the Omicron variant may emerge in 2022.

However, antivaccine sentiment, fuelled in part by organized disinformation efforts, has resulted in suboptimal uptake of readily available vaccines in many countries, with adverse health and economic consequences. 8–10

Although the decision not to receive vaccination is often framed in terms of the rights of individuals to opt out, 11.12 such arguments neglect the potential harms to the wider community that derive from poor vaccine uptake.

Nonvaccination is expected to result in amplification of disease transmission in unvaccinated subpopulations, but the communicable nature of infectious diseases means that this also heightens risk for vaccinated populations, when vaccines confer imperfect immunity. Although assortative (like-with-like) mixing 13 is characteristic of many communicable disease systems and may be expected to limit interaction between vaccinated and unvaccinated subpopulations to some degree, the normal functioning of society means that complete like-with-like mixing is not observed in reality. Furthermore, the airborne spread of SARS-CoV-2 14–20 means that close-range physical mixing of people from vaccinated and unvaccinated groups is not necessary for between-group disease transmission.

Historically, behaviours that create health risks for the community as well as individuals have been the subject of public health regulation. This is true of communicable infectious diseases but also applies to public health statutes

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

Simple mathematical models can often provide important insignts into the behaviour of complex communicable diseases systems. 13.24.25 To better understand the implications of the interplay between vaccinated and unvaccinated populations under different assumptions about population mixing, we constructed a simple susceptible—infectious—recovered model to reproduce the dynamics of interactions between vaccinated and unvaccinated subpopulations in a predominantly vaccinated population. We sought to contrast contribution to epidemic size and risk estimates by subpopulation, and to understand the impact of mixing between vaccinated and unvaccinated groups on expected disease dynamics.

Methods

Model

We constructed a simple compartmental model of a respiratory viral disease. 26 The model is described in Appendix 1 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.212105/tab-related-content). People are represented as residing in 3 possible "compartments:" susceptible to infection (S), infected and infectious (I), and recovered from infection with immunity (R). We divided the compartments to reflect 2 connected subpopulations: vaccinated and unvaccinated people. Susceptible people move into the infectious compartment after effective contacts (i.e., contacts of a nature and duration sufficient to permit transmission) with people who are infected. In the context of an airborne virus like SARS-CoV-2,14-20 effective contact may be conceptualized as "sharing air" with an infective case. After an infectious period, infectious people with SARS-CoV-2 recover with immunity. We also assumed that some fraction of the unvaccinated population had immunity at baseline owing to previous infection and that a fraction of the population was vaccinated. We treated immunity after vaccination as an all-or-none phenomenon, with a fraction of vaccinated people (as defined by vaccine effectiveness) entering the model in the immune state and the remainder being left in the susceptible state. For example, a vaccine that is 80% efficacious would result in 80% of vaccinated people becoming immune, with the remaining 20% being susceptible to infection. We did not model waning immunity.

Humans do not mix randomly and exhibit a tendency to interact preferentially with others like themselves, 13.27 a phenomenon referred to as "assortativity." The relative frequency of interactions between people within different groups occurs on a spectrum that lies between high assortativity (i.e., like-with-like mixing) and random mixing. For instance, age-assortative mixing is frequently observed; children are more likely to interact with other children than would be expected if contacts occurred at random across all age groups. The use of matrices to govern such interactions are described in Appendix 1.

However, with respect to contacts between people from 2 different groups, relative frequency of contacts will depend

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

20% of the population unvaccinated, when random mixing is assumed ($\eta = 0$), 20% of the contacts a vaccinated person has would be expected to occur with unvaccinated people. When exclusively like-with-like mixing is assumed ($\eta = 1$), 0% of contacts a vaccinated person has would be with unvaccinated people. For intermediate levels of likewith-like mixing ($\eta = 0.5$), 10% of a vaccinated person's contacts would be with unvaccinated people.

We otherwise parameterized our base case model to represent a disease similar to SARS-CoV-2 infection with Delta variant, with a reproduction number of an infectious disease in the absence of immunity or control (R_0) of 6,²⁸ and we used higher values to capture the dynamics of the Omicron variant.²⁹ Our lower-bound estimate for vaccine effectiveness (40%) reflected uncertainty about the emerging Omicron variant,^{3,7} whereas our upper bound (80%) reflected the higher effectiveness seen with the Delta variant.³⁰ Base case parameters, plausible ranges and relevant references are presented in Table 1.

Table 1: View inline

Model parameters

We used the model to explore the impact of varying rates of immunization and different levels of like-with-like mixing on the dynamics of disease in vaccinated and unvaccinated subpopulations. We evaluated the absolute contribution to overall case counts by these subpopulations, and within-group and overall infection risk. We calculated attack rates as the cumulative number of infections divided by the population size. We calculated a quantity (ψ), which we defined as the fraction of all infections among vaccinated people that derived from contact with unvaccinated people, divided by the fraction of all contacts that occurred with unvaccinated people. Effectively, this represents a normalized index of the degree to which risk in one group may be disproportionately driven by contact with another. For example, if 10% of contacts among vaccinated people are with unvaccinated people, but 50% of infections among vaccinated people derive from these contacts, ψ would have a value of 5. If infection were simply a function of frequency of contact between the groups and prevalence was the same across groups, ψ would have a value of 1. The value of ψ would increase above 1 either because of an increased fraction of infections derived from contact with unvaccinated people or a decrease in the amount of contact between the groups (i.e., an increase in like-with-like mixing).

A version of the model in Microsoft Excel is available at 10.6084/m9.figshare.15189576.

Ethics approval

Because this study involved the use of publicly available aggregate data, approval by a research ethics board was not required.

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

We present simulated epidemics that assume different amounts of mixing between vaccinated and unvaccinated groups in Figure 1. With 20% baseline immunity among unvaccinated people and 80% of the population vaccinated, we found that the absolute number of cases from vaccinated and unvaccinated groups was similar when mixing was random; however, after we adjusted for the substantially larger population in the vaccinated group, the risk of infection was markedly higher among unvaccinated people during the epidemic. With increased like-with-like mixing, differences in incidence between the vaccinated and unvaccinated groups became more apparent, with cases in the unvaccinated subpopulation accounting for a substantial proportion of infections during the epidemic wave. Like-with-like mixing uncoupled the dynamics of vaccinated and unvaccinated subpopulations, with unvaccinated subpopulations having higher and earlier peak incidence than vaccinated subpopulations. For example, with random mixing, peak incidence was simultaneous in the vaccinated and unvaccinated groups, but with strong like-with-like mixing the epidemic peak among vaccinated people occurred about 1 week later than among unvaccinated people; population-adjusted peak incidence was 4 times higher in the unvaccinated population than in the vaccinated population with random mixing, but about 30 times higher with strong like-with-like mixing (Figure 1).

oopulation with random mixing, but about 30 times nigher with strong like-with-like mixing (gens) .				
	Download figure			
	Open in new tab			

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

Figure SCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 30 of 95

Simulated epidemics for different levels of mixing between vaccinated and unvaccinated populations. (A, C, E) Incident cases and (B, D, F) population-adjusted incidence per 100 population in unvaccinated, vaccinated and overall modelled populations. The degree of like-with-like mixing (assortativity, η) varies from (A, B) random mixing (η = 0) to (C, D) intermediate like-with-like mixing (η = 0.5) to (E, F) near exclusive mixing with people of the same vaccination status (η = 0.9). As like-with-like mixing increases, epidemic size among the vaccinated subpopulation is smaller in absolute terms than among the unvaccinated subpopulation and also has a different contour. (G) Increasing like-with-like mixing increased cumulative attack rates among unvaccinated people and decreased cumulative attack rates among vaccinated people. The highest overall attack rates were seen with intermediate levels of like-with-like mixing.

We found that cumulative attack rates among vaccinated people were highest (15%) with random mixing and lowest (10%) with highly assortative mixing. In contrast, cumulative attack rates were lowest (62%) among unvaccinated people with random mixing, and highest (79%) with highly assortative mixing. The highest cumulative attack rates in the population overall were seen with intermediate levels of like-with-like mixing (27%) compared with random mixing (25%) and strong like-with-like mixing (24%) (Figure 1).

When we varied the degree of like-with-like mixing, changes in epidemic size in the vaccinated subpopulation occurred. As like-with-like mixing increased (i.e., with reduced contact between vaccinated and unvaccinated subpopulations), the final attack rate decreased among vaccinated people, but the contribution of risk to vaccinated people caused by infection acquired from contact with unvaccinated people (as measured by ψ) increased. The larger the value of ψ , the more unvaccinated people contributed to infections in the vaccinated subpopulation.

This pattern was consistent across a range of values for vaccine effectiveness and reproduction numbers (Figure 2). We found that increased like-with-like mixing reduced final outbreak size among vaccinated people most markedly at lower reproduction numbers but increased the value of ψ. With lower vaccine effectiveness, as observed with the Omicron variant, the effects of like-with-like mixing were attenuated. With either lower reproduction numbers or higher vaccine efficacy, transmission was more readily disrupted within the vaccinated subpopulation, such that risk arose increasingly from interactions with the unvaccinated subpopulation, where transmission continued. As like-with-like mixing increased, contribution to infection risk among vaccinated people was increasingly derived from (less and less common) interactions with unvaccinated people, increasing the value of ψ. We found similar patterns in sensitivity analyses in which vaccine coverage was increased from 80% to 99% (Figure 3). Increasing population vaccination coverage decreased the attack rate among vaccinated people (as expected, owing to indirect protective effects) but further increased the relative contribution to risk in vaccinated people by those who were unvaccinated at any level of like-with-like mixing.

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

USCA11 Case: 21-12729	Document: 44-2	Date Filed: 10/06/2022	Page: 31 of 95
	Download	figure	
	Open in ne	ew tab	
	Download po	werpoint	
Figure 2: Impact of mixing between vaccinated and a reproduction numbers and (B) vaccine effe size among the vaccinated subpopulation a people (ψ). As like-with-like mixing (η) increases seen across a range of (A) initial reproduction reproduction numbers and are attenure reproduction number in the sensitivity analysis for <i>R</i> .	ctiveness. Both panels shand contact-adjusted control eases, the attack rate amountion numbers and (B) valuated as vaccines become	ow the impact of increasing like-with ribution to risk of infection in vaccinous vaccinated people decreases, but it is effectiveness. These effects are less effective. We used a base ca	h-like mixing on outbreak ated people by unvaccinated out ψ increases. This relation are more pronounced at se estimate of 6 for the
Ve use cookies on this site to enhance	e your user experience	e. By clicking any link on this p	age you are giving your

Continue

Find out more

consent for us to set cookies.

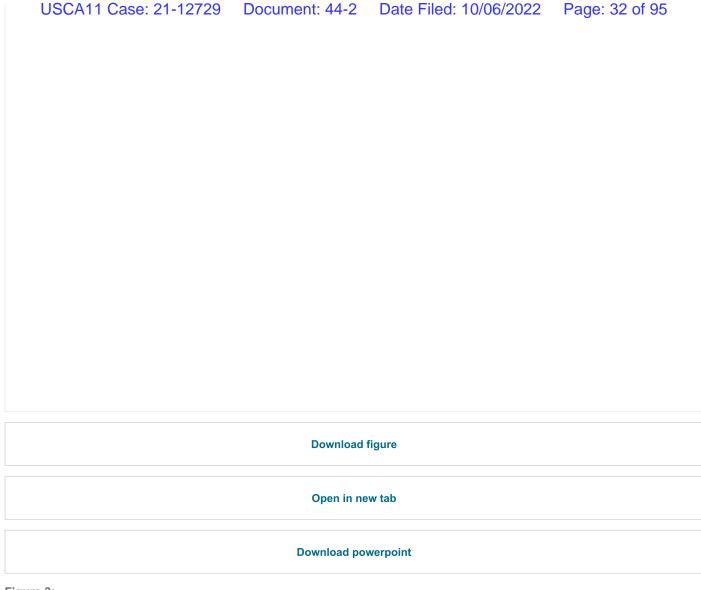


Figure 3:

Impact of mixing between vaccinated and unvaccinated subpopulations on contribution to risk and final epidemic size with increasing population vaccination coverage. Increasing population vaccination coverage decreases the attack rate among vaccinated individuals and further increases the relative contribution to risk in vaccinated individuals by the unvaccinated at any level of like-with-like mixing. For levels of vaccination coverage that were evaluated, increasing like-with-like mixing decreases the attack rate among the vaccinated but increases the relative contribution to risk in vaccinated individuals by the unvaccinated.

Interpretation

We use a simple deterministic model to explore the impact of assortative mixing on disease dynamics and contribution to risk in a partially vaccinated population during a pandemic modelled on the current pandemic of SARS-CoV-2. Notwithstanding the model's simplicity, it provides a graphical representation of the expectation that even with highly effective vaccines, and in the face of high vaccination coverage, a substantial proportion of new

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

differentially interact with others who are like themselves is likely to have an important impact on disease dynamics and on risk in people who choose to get vaccinated.

Vaccinated people were, as expected, at markedly lower risk of SARS-CoV-2 infection during the epidemic; however, when random mixing with unvaccinated people occurred, they decreased attack rates in the unvaccinated people, by serving as a buffer to transmission. As populations became more separate with progressively increasing like-with-like mixing, final epidemic sizes declined in vaccinated people, but rose in unvaccinated people because of the loss of buffering via interaction with vaccinated people. Many opponents of vaccine mandates have framed vaccine adoption as a matter of individual choice. However, we found that the choices made by people who forgo vaccination contribute disproportionately to risk among those who do get vaccinated.

Increased mixing between vaccinated and unvaccinated groups increased final epidemic size among vaccinated people; conversely, more like-with-like mixing decreased final epidemic size among vaccinated people but resulted in enhancement of the degree to which risk among vaccinated people could be attributed to unvaccinated people. The fact that this excess contribution to risk cannot be mitigated by high like-with-like mixing undermines the assertion that vaccine choice is best left to the individual and supports strong public actions aimed at enhancing vaccine uptake and limiting access to public spaces for unvaccinated people, because risk cannot be considered "self-regarding." 35 There is ample precedent for public health regulation that protects the wider community from acquisition of communicable diseases, even if this protection comes at a cost of individual freedom. 36.37 We also note that the use of legal and regulatory tools for the prevention of behaviours and practices that create risk for the wider public also extend beyond communicable infectious diseases, such as statutes that limit indoor cigarette smoking. 21–23

In the context of immune evasion seen with the newly emerged Omicron variant, we found that like-with-like mixing is less protective when vaccine effectiveness is low. This finding underlines the dynamic nature of the pandemic, and the degree to which policies need to evolve in a thoughtful manner as the nature of the disease and the protective effects of vaccines evolve. Boosting with mRNA vaccines appears to restore vaccine effectiveness at least temporarily against Omicron, and it is likely that the higher vaccine effectiveness estimates used in our model will be relevant to public policy as booster campaigns are scaled up in Canada and elsewhere.

Despite reduced protection against infection by the Omicron variant, vaccinated people, including those who have not received third vaccine doses, have continued to receive strong protection against admission to hospital and death from SARS-CoV-2 infection. This means that acceptance of vaccination is a means of ensuring that greater health care capacity is available for those with other illnesses. For example, in Ontario, capacity for COVID-19 cases in intensive care units was created by cancelling elective surgeries for cancer and cardiac disease, which

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

The robustness of our findings in the face of wide-ranging sensitivity analysis will allow this work to be applied in the future, when new variants arise, as we understand the length of time vaccination confers immunity and as new vaccine formulations become available.

Limitations

The simplicity of our model is both a strength (it is transparent and easily modified to explore the impact of uncertainty) and a weakness, because it does not precisely simulate a real-world pandemic process in all its complexity. For instance, we modelled vaccine effectiveness against infection but not the additional benefits of vaccination for preventing severe illness. Although this benefit is not captured by a simple model focused on transmission, an advantage of models such as ours is that they provide a ready platform for layering on increasing complexity, so our model can be adapted or expanded to consider impacts on the health system, or to incorporate additional structural elements or alternate assumptions. We have also likely underestimated vaccine benefit in this model, as we have not attempted to capture the impact of vaccines on prevention of forward transmission by vaccinated, infected individuals; this effect appears to be substantial.

Conclusion

Using simple mathematical modelling, we have shown that, although risk associated with avoiding vaccination during a virulent pandemic accrues chiefly to those who are unvaccinated, the choice of some individuals to refuse vaccination is likely to affect the health and safety of vaccinated people in a manner disproportionate to the fraction of unvaccinated people in the population. Risk among unvaccinated people cannot be considered self-regarding, and considerations around equity and justice for people who do choose to be vaccinated, as well as those who choose not to be, need to be considered in the formulation of vaccination policy. It is unlikely that SARS-CoV-2 will be eliminated, and our findings will likely be relevant to future seasonal SARS-CoV-2 epidemics or in the face of emerging variants.

Footnotes

- Competing interests: David Fisman has served on advisory boards related to influenza and SARS-CoV-2 vaccines for Seqirus, Pfizer, AstraZeneca and Sanofi-Pasteur Vaccines, and has served as a legal expert on issues related to COVID-19 epidemiology for the Elementary Teachers Federation of Ontario and the Registered Nurses Association of Ontario. He also served as a volunteer scientist on the Ontario COVID-19 Science Advisory Table. Ashleigh Tuite was employed by the Public Health Agency of Canada when the research was conducted. The work does not represent the views of the Public Health Agency of Canada. No other competing interests were declared.
- This article has been neer reviewed

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

- Funding: This research was supported by a grant from the Cartad and stitutes of Health Research (tof 95 David Fisman; 2019 COVID-19 rapid researching funding OV4-170360). The funder had no direct role in this work.
- **Data sharing:** A version of the model in Microsoft Excel is freely available at 10.6084/m9.figshare.15189576.

Accepted March 23, 2022.

This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: https://creativecommons.org/licenses/by-nc-nd/4.0/

References

- 1. «Kreier F. 'Unprecedented achievement': who received the first billion COVID vaccinations? *Nature* 2021 Apr. 29 [Epub ahead of print]. doi: 10.1038/d41586-021-01136-2. <u>CrossRef Google Scholar</u>
- 2. Mancuso M, Eikenberry SE, Gumel AB. Will vaccine-derived protective immunity curtail COVID-19 variants in the US? *Infect Dis Model* 2021;6:1110–34. CrossRef Google Scholar
- 3.

 SARS-CoV-2 variants of concern and variants under investigation in England. Technical Briefing 31. London (UK): UK Health Security Agency; 2021. Available:

 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040076/Technical_Briefing_31.pdf (accessed 2021 Dec. 13). Google Scholar
- 4. Oliu-Barton M, Pradelski BSR, Algan Y, et al. Elimination versus mitigation of SARS-CoV-2 in the presence of effective vaccines. *Lancet Glob Health* 2022;**10**: e142–e147. Google Scholar
- 5. Garcia-Beltran WF, StDenis KJ, Hoelzemer A, et al. mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. *Cell* 2022;**185**:457–66. Google Scholar
- 6. Roland D. Covid-19 vaccine makers are unsure if fine-tuning shots for Omicron is worthwhile. researchers question whether 'original antigenic sin' applies to the new variant. Wall Street Journal [New York] 2021 Dec. Available: https://www.wsj.com/articles/covid-19-vaccine-makers-are-unsure-if-fine-tuning-shots-for-omicron-is-worthwhile-11639054806 (accessed 2021 Dec. 17). Google Scholar
- 7. Hogan AB, Wu SL, Doohan P, et al. Report 48 The value of vaccine booster doses to mitigate the global impact of the Omicron SARS-CoV-2 variant. London (UK): Imperial College London; 2021. Available: http://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-48-global-omicron/ (accessed 2021 Dec. 17). Google Scholar
- 8. Rovetta A. The impact of COVID-19 on conspiracy hypotheses and risk perception in Italy: infodemiological survey study

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue Find out more

- 10. Basch CH, Meleo-Erwin Z, Fera J, et al. A global pandemic in the time of viral memes: COVID-19 vaccine misinformation and disinformation on TikTok. Hum Vaccin Immunother 2021;17:2373–7. Google Scholar
- 11. Hollingsworth P, Van Horne R. 'There's quite a bit of scope to do this in a time of pandemic' legal expert says of vaccine mandates. CTV News 2021 Oct. 8. Available: https://atlantic.ctvnews.ca/there-s-quite-a-bit-of-scope-to-do-this-in-a-time-of-pandemic-legal-expert-says-of-vaccine-mandates-1.5617486 (accessed 2021 Nov. 16). Google Scholar
- 12. d Delgado J. Republicans pitch stripping Surgeon General of vaccine mandate power. *Florida Politics* 2021 Nov. 16. Available: https://floridapolitics.com/archives/473253-republicans-pitch-stripping-surgeon-general-of-vaccine-mandate-power/ (accessed 2021 Nov. 16). Google Scholar
- 13. Garnett GP, Anderson RM. Sexually transmitted diseases and sexual behavior: insights from mathematical models. *J Infect Dis* 1996;**174**(Suppl 2):S150–61. CrossRef PubMed Google Scholar
- 14. Peng Z, Rojas ALP, Kropff E, et al. Practical indicators for risk of airborne transmission in shared indoor environments and their application to COVID-19 outbreaks. *Environ Sci Technol* 2022;**56**:1125–37. Google Scholar
- 15. Tang JW, Bahnfleth WP, Bluyssen PM, et al. Dismantling myths on the airborne transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *J Hosp Infect* 2021;**110**:89–96. CrossRef PubMed Google Scholar
- 16. Marr LC, Tang JW. A paradigm shift to align transmission routes with mechanisms. *Clin Infect Dis* 2021;**73**:1747–9. Google Scholar
- 17. Samet JM, Prather K, Benjamin G, et al. Airborne transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): what we know. *Clin Infect Dis* 2021;**73**:1924–6. <u>Google Scholar</u>
- 18. Prather KA, Marr LC, Schooley RT, et al. Airborne transmission of SARS-CoV-2. *Science* 2020;**370**:303–4. <u>FREE Full Text</u> <u>Google Scholar</u>
- 19. Morawska L, Tang JW, Bahnfleth W, et al. How can airborne transmission of COVID-19 indoors be minimised? *Environ Int* 2020;**142**:105832. CrossRef PubMed Google Scholar
- 20. d'Hawks SA, Prussin AJ II., Kuchinsky SC, et al. Infectious SARS-CoV-2 is emitted in aerosol particles. *MBio* 2021;**12**:e0252721. Google Scholar
- 21. Fishman JA, Allison H, Knowles SB, et al. State laws on tobacco control United States, 1998. *MMWR CDC Surveill Summ* 1999;**48**:21–40. Google Scholar
- 22. Morain S, Largent E. Ethical acceptability of reducing the legal blood alcohol concentration limit to 0.05. *Am J Public Health* 2019;**109**:709–13. Google Scholar
- 23. Wiens T, Lenk KM, Fabian LEA, et al. Law enforcement practices in the first two states in U.S. to legalize recreational marijuana. *Int J Drug Policy* 2018;**61**: 38–43. Google Scholar

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

- 25. Dushoff J, Plotkin JB, Levin SA, et al. Dynamical resonance can account for seasonality of influenza epidemics. *Proc Natl Acad Sci U S A* 2004;**101**:16915–6. Abstract/FREE Full Text. Google Scholar
- 26. Tuite AR, Fisman DN, Greer AL. Mathematical modelling of COVID-19 transmission and mitigation strategies in the population of Ontario, Canada. *CMAJ* 2020;**192**:E497–505. Abstract/FREE Full Text Google Scholar
- 27. Béraud G, Kazmercziak S, Beutels P, et al. The French Connection: the first large population-based contact survey in France relevant for the spread of infectious diseases. *PLoS One* 2015;**10**:e0133203. CrossRef PubMed Google Scholar
- 28. ⁴Xia F, Yang X, Cheke RA, et al. Quantifying competitive advantages of mutant strains in a population involving importation and mass vaccination rollout. *Infect Dis Model* 2021;**6**:988–96. <u>Google Scholar</u>
- 29. Nishiura H, Ito K, Anzai A, et al. Relative reproduction number of SARS-CoV-2 Omicron (B.1.1.529) compared with Delta variant in South Africa. *J Clin Med* 2021;**11**:30. Google Scholar
- 30. Risk M, Shen C, Hayek SS, et al. Comparative effectiveness of COVID-19 vaccines against the Delta variant. Clin Infect Dis 2022 Feb. 7;ciac106 [Epub ahead of print]. doi: 10.1093/cid/ciac106. CrossRef Google Scholar
- 31. Wolfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;**581**:465–9. CrossRef PubMed Google Scholar
- 32. Little N. COVID-19 vaccination tracker. *COVID19Tracker.ca* 2021. Available: https://covid19tracker.ca/vaccinationtracker.html (accessed 2021 Dec. 10). Google Scholar
- 33. Higdon MM, Wahl B, Jones CB, et al. A systematic review of COVID-19 vaccine efficacy and effectiveness against SARS-CoV-2 infection and disease. *medRxiv* 2021 Sept. 25 [preprint].doi: https://doi.org/10.1101/2021.09.17.21263549. Google Scholar
- 34. *Population estimates, quarterly. Table: 17-10-0009-01 (formerly CANSIM 051-0005*). Ottawa: Statistics Canada. Available: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901 (accessed 2020 May 29). **Google Scholar**
- 35. 4 Sleat D, Innes K, Parker I. Are vaccine passports and COVID passes a valid alternative to lockdown? *BMJ* 2021;**375**:n2571. FREE Full Text Google Scholar
- 36. Lerner BH. Catching patients: tuberculosis and detention in the 1990s. *Chest* 1999;**115**:236–41. CrossRef PubMed Google Scholar
- 37. Dyer O. Ontario suspends unvaccinated children from school and proposes mandatory classes for parents. *BMJ* 2015;**351**:h6821. FREE Full Text Google Scholar
- 38. & COVID-19 vaccine surveillance report: week 5, February 3, 2022. London (UK): UK Health Security Agency; 2022. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1052353/Vaccine_surveillance report week 5.pdf (accessed 2022 Feb. 8). Google Scholar
- 39. Thompson MG, Natarajan K, Irving SA, et al. Effectiveness of a third dose of mRNA vaccines against COVID-19-associated We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue Find out more

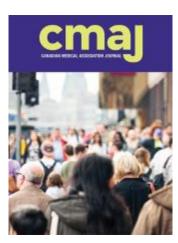
- 40. Prescription for Ontario: Doctors 5-point plan for better health care. Toronto: Ontario Medical Association; 2021. Available: https://www.oma.org/uploadedfiles/oma/media/public/prescription-for-ontario-doctors-5-point-plan-for-better-health-care.pdf (accessed 2022 Feb. 8). Google Scholar
- 41. ⁴Lyngse FP, Mortensen LH, Denwood MJ, et al. SARS-CoV-2 Omicron VOC transmission in Danish households. *medRxiv* 2022 Jan. 30 [preprint]. doi: https://doi.org/10.1101/2022.01.28.22270044. Google Scholar



Next 🗪

▲ Back to top

In This Issue



CMAJ Vol. 194, Issue 16 25 Apr 2022 Table of Contents Index by author

Article Tools

Respond to this article
₽rint
▲ Download PDF
Article Alerts
Email Article
Citation Tools
© Request Permissions
♠ Share

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 39 of 95

▼ Related Articles

Error in key model input

Study authors don't consider waning SARS-CoV-2 immunity after vaccination in their model

The authors respond to criticisms of their model parameters

PubMed Google Scholar

▶ Cited By...

▶ More in this TOC Section

Collections

Areas of Focus

Health services

Topics

Epidemiology & epidemiological methods

Health policy

Infectious diseases

Infectious diseases: COVID-19

Public health

Vaccination



We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

View the latest classified ads from CMAJ

_	4		- 4
100	MT	ΔI	വ
\sim	7 H H L	U	

Current issue

Past issues

Collections

Sections

Blog

Podcasts

Alerts

RSS

Early releases

Information for

Advertisers

Authors

Reviewers

CMA Members

CPD credits

Media

Reprint requests

Subscribers

About

General Information

Journal staff

Editorial Board

Advisory Panels

Governance Council

Journal Oversight

Careers

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue

CMA Civing Standards: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 41 of 95

Copyright 2022, CMA Impact Inc. or its licensors. All rights reserved. ISSN 1488-2329 (e) 0820-3946 (p)

All editorial matter in CMAJ represents the opinions of the authors and not necessarily those of the Canadian Medical Association or its subsidiaries.

To receive any of these resources in an accessible format, please contact us at CMAJ Group, 500-1410 Blair Towers Place, Ottawa ON, K1J 9B9; p: 1-888-855-2555; e: cmajgroup@cmaj.ca

We use cookies on this site to enhance your user experience. By clicking any link on this page you are giving your consent for us to set cookies.

Continue



CDC Newsroom Home

COVID-19 vaccines continue to protect against hospitalization and death among adults

Media Statement

For Immediate Release: Friday, March 18, 2022

Contact: Media Relations

(404) 639-3286

COVID-19 vaccines continue to protect against hospitalization and death among adults

COVID-19 vaccination continues to help protect adults against severe illness with COVID-19, including hospitalizations and death, according to two reports released in today's *MMWR*.

During Omicron, COVID-19-associated hospitalization rates increased for all adults, regardless of vaccination status, but rates were 12 times higher among adults who were unvaccinated compared to adults who received a booster or additional doses. Hospitalization rates were also highest among non-Hispanic Black adults and nearly 4 times as high among Black adults than White adults during the peak of Omicron.

Additionally, mRNA vaccines continued to be highly effective at protecting against COVID-19-associated ventilation or death, including during the Omicron period. Protection was highest in adults who received a third vaccine dose, reducing the risk for COVID-19-associated ventilation or death during the Omicron period by 94%.

CDC continues to recommend that everyone 5 years and older stay up to date on their COVID-19 vaccines, including a booster dose for those who are eligible. We also must work to ensure everyone has equitable access to vaccines and treatments by focusing efforts on reaching people who have been disproportionately affected, so that they can be protected from the effects of the virus, including severe illness, hospitalization, and death.

CDC works 24/7 protecting America's health, safety and security. Whether disease start at home or abroad, are curable or preventable, chronic or acute, or from human activity or deliberate attack, CDC responds to America's most pressing health threats. CDC is headquartered in Atlanta and has experts located throughout the United States and the world.

Page last reviewed: March 18, 2022

Home > Coronavirus (COVID-19)

Press release

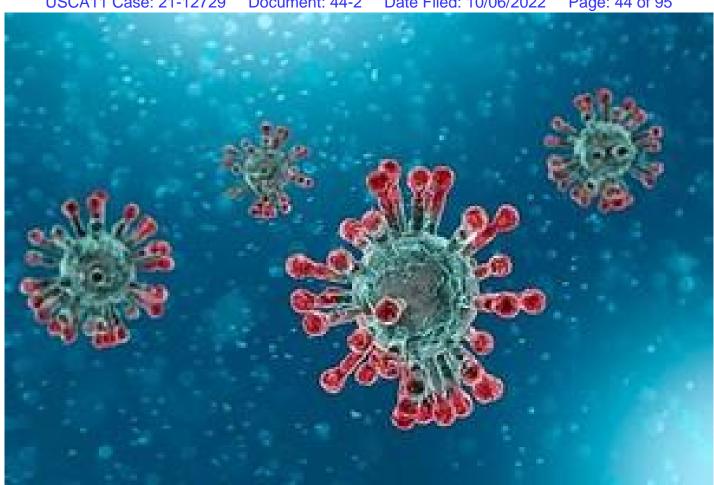
UKHSA review shows vaccinated less likely to have long COVID than unvaccinated

A new review by UKHSA shows that people who have had one or more doses of a coronavirus (COVID-19) vaccine are less likely to develop long COVID than those who remain unvaccinated.

From:

UK Health Security Agency (/government/organisations/uk-health-security-agency)

Published 15 February 2022 USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 44 of 95



The UK Health Security Agency (UKHSA) has undertaken a rapid evidence review looking at the effects of vaccination against long COVID or post-COVID symptoms. The review includes 15 UK and international studies that were undertaken up until January 2022.

An estimated 2% of the UK population have reported symptoms of long COVID or post-COVID syndrome, which can last for more than 4 weeks after their initial infection. The 3 most common symptoms are fatigue, shortness of breath and muscle or joint pain.

Eight of the studies in the review looked at the effect of vaccinations administered before infection. Most of these studies suggest that vaccinated people (one or 2 doses) were less likely to develop symptoms of long COVID following infection compared with unvaccinated people – in the short term and long term (4 weeks up until 6 months after infection).

The data from some of the studies included in the review suggests that:

people with COVID-19 who received 2 doses of the Pfizer, AstraZeneca, or Moderna vaccines or one dose of the Janssen vaccine, were about half as likely as people who received one dose or were unvaccinated to develop long COVID symptoms lasting more than 28 days

vaccine effectiveness against most post-COVID symptoms in adults was highest in people aged 60 years and over, and lowest for younger participants (19 to 35 years)

The remaining studies looked at the effects of vaccination among people who already had long COVID symptoms.

Four studies specifically compared long COVID symptoms before and after vaccination. Three of these studies suggested that more people with COVID-19 reported an improvement than a worsening in symptoms after vaccination, either immediately or over several weeks.

Another 3 studies of unvaccinated people with long COVID compared ongoing symptoms in those who either went on to receive a vaccination or remained unvaccinated. These studies suggested that those who were vaccinated were less likely to report long COVID symptoms after vaccination than people who remained unvaccinated over the same period.

One study looked specifically at the timing of vaccination after COVID-19 infection and suggested that people with COVID-19 who were vaccinated sooner after diagnosis were much less likely to report long COVID symptoms than people who were vaccinated later after diagnosis. All studies were observational, so results may be from differences other than vaccination.

In one study, of those participants who reported having long COVID, a greater proportion of vaccinated participants said their symptoms improved compared to unvaccinated participants (23.2% compared to 15.4% respectively).

Dr Mary Ramsay, Head of Immunisation at UKHSA, said:

- "These studies add to the potential benefits of receiving a full course of the COVID-19 vaccination. Vaccination is the best way to protect yourself from serious symptoms when you get infected and may also help to reduce the longer-term impact.
- " For most people symptoms of long COVID are short-lived and resolve overtime. But for some, symptoms can be more severe and disrupting to their daily lives.
- " If you're experiencing unusual symptoms particularly for longer than 4 weeks after infection, you should consider contacting your GP."

The review concluded that people who received 2 doses of a vaccine against COVID-19 were less likely to develop long COVID symptoms or experience symptoms for a shorter time, compared with those unvaccinated.

Individuals who received a vaccination after being infected with COVID-19 also reported that the duration of post-COVID symptoms was less than for those who were unvaccinated. Two doses of the COVID-19 vaccination provide a high level of

UK Health Security Agency press office

Nobel House 17 Smith Square London SW1P 3JR

Email

phe-pressoffice@phe.gov.uk

Telephone 020 7654 8400

Out of hours 020 8200 4400

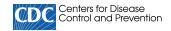
Explore the topic

Coronavirus (COVID-19) (/coronavirus-taxon)

OGL

All content is available under the <u>Open Government Licence</u> <u>v3.0</u>, except where otherwise stated

© Crown copyright





COVID-19

Cruise Ship Travel During COVID-19

Updated July 18, 2022

CDC is reviewing this page to align with updated guidance.



As of July 18, 2022, CDC's COVID-19 Program for Cruise Ships is no longer in effect. CDC will continue to publish guidance to help cruise ships continue to provide a safer and healthier environment for passengers, crew and communities going forward. For more information, please see the Frequently Asked Questions (FAQs).

What You Need to Know

- Check if you are up to date with your COVID-19 vaccines before cruise ship travel.
- If you have a medical condition or are taking medication that weakens your immune system, you might NOT be fully
 protected even if you are up to date with your COVID-19 vaccines. Talk to your healthcare provider about your risk
 before travel. Even after vaccination, you may need to continue taking precautions.
- The virus that causes COVID-19 spreads easily between people in close quarters on board ships. If the virus is spreading on board a cruise ship, passengers and crew are at risk for infection.
- Check directly with your cruise line about their testing or vaccination protocols before travel.
- If your cruise line does not have a testing requirement, get tested for current infection with a COVID-19 viral test as close to time of cruise departure as possible (no more than 3 days before you travel).
- Get tested again with a COVID-19 viral test 3-5 days after your cruise.

Before Cruise Travel

Do not travel or board a cruise ship if...

- You are sick with COVID-19.
- You tested positive for COVID-19 less than 10 days ago (day 0 is the day your symptoms started or the day your positive test sample was taken if you had no symptoms).
- You had close contact with a person with COVID-19 in the past 5 days and are recommended to quarantine.
 - Get tested at least 5 days after your last close contact. Make sure your test result is negative and you remain without symptoms before traveling.
 - Properly wear a well-fitting mask when you are around others through day 10. If you are unable to wear a mask, you should not travel during this time.

Check with your cruise line regarding their policies.

- Be up to date with your COVID-19 vaccines before travel.
- Check if your cruise line requires proof of vaccination or pre-embarkation testing, or has any other requirements to board.
- If traveling by air before or after cruise travel, check if your airline or destination (see here for U.S. requirement) requires any testing, vaccination, or other documents.
- Consider getting travel insurance. Consider buying additional insurance that covers health care and emergency evacuation, especially if you will be traveling to remote areas. Make sure you have a plan to get care overseas, in case you need it.



Pre-embarkation Testing

- If your cruise line does not have a testing requirement, get tested for current infection with a viral test (no more than 3 days) before boarding a cruise ship, regardless of your vaccination status. Get your test results before you board your cruise.
 - If you recovered from COVID-19 in the past 90 days, testing is not generally recommended unless you
 have symptoms. People can continue to test positive for up to 90 days after diagnosis and not be
 infectious to others. Check with your cruise line regarding their specific policies, including if you need to
 provide a copy of your positive test result and a letter from your healthcare provider documenting that
 you recovered from COVID-19.
- If you or your travel companions have COVID-19 symptoms or test positive at embarkation, the cruise ship may deny you from boarding. If you are allowed to board, you may be required to isolate or quarantine, depending on your symptoms and test results.

During Cruise Travel



Protect Yourself and Others

- Wash your hands often with soap and water or use hand sanitizer with at least 60% alcohol.
- Follow recommendations for protecting yourself and others.
- If you have symptoms of COVID-19, stay in your cabin and notify the onboard medical center immediately. It's important to report your symptoms, even if they are mild, to protect others on board including passengers at increased risk for severe illness and crew.



Masks

- Follow any ship-specific mask protocols.
- Follow CDC's recommendations for wearing masks in travel and public transportation settings.

If You Develop Symptoms or Use a Self-Test on Board with a Positive Result

- · Isolate yourself in your cabin immediately.
- Call your ship's medical center.

Cruise ships may have their own requirements for testing, isolation, quarantine, mask wearing, and dining for people with COVID-19 or their close contacts. If you have questions about a cruise ship's specific policies, please contact them directly.

• If you disembark the ship before completing your isolation or quarantine period, you should follow CDC's guidance, or local guidance if you disembark in another country.

After Cruise Travel

- Self-monitor for COVID-19 symptoms.
 - Follow additional guidance if you know you were exposed to a person with COVID-19.

• Get tested Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 49 of 95 Get tested Case: 3-5 days after your trip or if you develop symptoms.

- Isolate if you develop symptoms or your test result is positive.
 - If your test result is positive, contact your state, territorial, local or tribal health department to tell them you have COVID-19 and recently traveled on a cruise ship.
- Follow all state, territorial, local or tribal recommendations or requirements after travel.

Frequently Asked Questions

What happened to CDC's COVID-19 Program for Cruise Ships?

CDC has worked closely with the cruise industry, state, territorial, and local health authorities, and federal and seaport partners to provide a safer and healthier environment for cruise passengers and crew. Cruise ships have access to guidance and tools to manage their own COVID-19 mitigation programs. Additionally, cruise travelers have access to recommendations that allow them to make informed decisions about cruise ship travel. While cruising poses some risk of COVID-19 transmission, CDC will continue to publish guidance to help cruise ships continue to provide a safer and healthier environment for crew, passengers, and communities going forward.

Why was the cruise ship color-coding system removed?

The previous color-coding system under CDC's COVID-19 Program for Cruise Ships depended upon each cruise line having the same COVID-19 screening testing standards, which may now vary among cruise lines. Therefore, the cruise ship color status webpage has been retired. CDC will continue to provide testing recommendations for cruise ship operators to follow and cruise ships will continue to report COVID-19 cases to CDC.

How can travelers find out about COVID-19 outbreaks on cruise ships?

Cruise travelers have the option of contacting their cruise line directly regarding outbreaks occurring on board their ship.

More Information

If you need to contact your health department: State & Territorial Health Department Websites

Guidance for Cruise Ships on the Mitigation and Management of COVID-19

Travel during the COVID-19 Pandemic

International Travel

Frequently Asked Questions and Answers for Travelers

Last Updated July 18, 2022



Insights Services Industries Careers About us

How COVID-19 impacted supply chains and what comes next

By Sean Harapko

8 minute read 18 Feb 2021

Research shows severe disruption through the pandemic is driving enterprises to make their supply chains more resilient, collaborative and networked.

he COVID-19 pandemic has posed significant challenges for supply chains globally. Multiple national lockdowns continue to slow or even temporarily stop the flow of raw materials and finished goods, disrupting manufacturing as a result. However, the pandemic has not necessarily created any new challenges for supply chains. In some areas, it brought to light previously unseen vulnerabilities, and of course, many organizations have suffered staff shortages and losses due to COVID-19. But overall, it has accelerated and magnified problems that already existed in the supply chain.

The following are some findings from a survey that Ernst & Young LLP (EY US) conducted in late 2020. The respondents were 200 senior-level supply chain executives at organizations across many sectors, including consumer products, retail, life sciences, industrial products, automotive, and high-tech companies in the United States with over US\$1b in revenues.

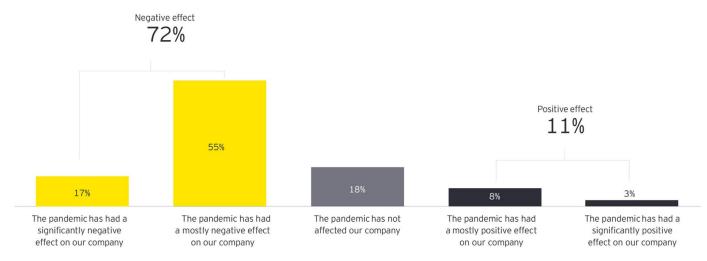
In the aftermath of severe disruption from the COVID-19 pandemic, the survey found that enterprises in the US plan to shake up their supply chain strategies to become more resilient, collaborative, and networked with customers, suppliers, and other stakeholders. To do that, they will increase investment in supply chain technologies like AI and robotic process automation while retraining workers.

Chapter 1

The pandemic had substantial negative effects on supply chains

Certain sectors fared worse than others, but some life sciences companies reported few effects.

The COVID-19 pandemic was a global disruption across trade, finance, health and education systems, businesses and societies like few others in the past 100 years. It is no surprise then that only 2% of companies who responded to the survey said they were fully prepared for the pandemic. Serious disruptions affected 57%, with 72% reporting a negative effect (17% reported a significant negative effect, and 55% mostly negative).



Often in uncertain economic environments, companies slow their technology investments to a trickle. But during the COVID-19 pandemic, 92% did not halt technology investments. This speaks to the value of a digital supply chain in helping enterprises navigate disruptive forces and respond faster to volatile supply and demand.

There were some clear winners by industry during the pandemic, with 11% reporting positive effects, including increased customer demand (71%) and bringing new products to market (57%). These companies were mostly in the life sciences sector and the positive effects may be largely because the products they produce are essential. The pandemic also required some life sciences companies to double down on creating essential new products such as COVID-19 tests or vaccines. Other sectors, particularly consumer products, couldn't keep products on the shelves in the early days of the pandemic since toilet paper, canned goods, flour

How EY can help

Smart Factory

EY Smart Factory arms your shop floor with dynamic predictive data analytics, virtual reality and artificial intelligence to deliver unprecedented performance.

Read more

and other staples were in high demand.

Some sectors were hit particularly hard, however. Among survey respondents, all automotive and nearly all (97%) industrial products companies said the pandemic has had a negative effect on them. In addition, 47% of all companies reported the pandemic disrupted their workforce. While many employees were asked to work from home, others — especially in factory settings — had to adapt to new requirements for physical spacing, contact-tracing and more personal protective equipment (PPE). Industrial products and high-tech manufacturing companies are investing overwhelmingly in technology to reduce employee exposure to COVID-19 in more labor-intensive industries. These are just a few examples of changes affecting supply chains across various sectors.

Chapter 2

Big changes are on the horizon for supply chains

Greater supply chain visibility, efficiency and resilience are top of mind.

The executive supply chain survey indicates that efficiency and reskilling supply chain workers will be top priorities in the next three years. These findings are not surprising as cost-optimization in the supply chain will always be a focus, even in the face of building out additional resiliency. The survey also shows that supply chain visibility becomes the number one priority over the next three years. This finding closely matches a **2019 EY supply chain survey** in which visibility ranked as the top factor in a successful supply chain.



With the need for increased visibility across typically hundreds or thousands of suppliers, we are already seeing a shift from linear supply chains to more integrated networks connecting many players. Enabling this sea change are technologies such as IoT devices or sensors that provide valuable data on where goods are in the chain and their condition — for example, products for which temperature monitoring may be critical (i.e., frozen foods, vaccines or other medicines).

With 61% of respondents saying they will retrain and reskill their workforce in the next year, there will be efforts to help workers use digital technologies, adapt to changing company strategies and ways of working like increased virtual collaboration, and assist people in operating equipment with health and safety in mind. Top workforce measures identified in the survey include increased automation (63%) and investments in AI and machine learning, with 37% of respondents already deploying these technologies and another 36% planning to use them soon.

It may be safe to assume that because of COVID-19, companies put their sustainability goals on hold in order

to manage through the pandemic. The survey found just the opposite -85% are more focused on environmental and sustainability goals (ESG). With investors seeking information on a company's ESG performance, employees wanting to work for companies with sustainability built into their mission statements, increased customer expectations for sustainability and increasing regulation from various countries, sustainable supply chain practices no doubt are here to stay.

Chapter 3

The future of supply chains is digital and autonomous

The journey to digitized and lights-out operation has begun in earnest.

The pandemic has indeed accelerated many preexisting trends, and supply chain is no exception: 64% of surveyed supply chain executives say digital transformation will accelerate due to the pandemic. The race is on for digital enablement and automation: 52% of executives say that the autonomous supply chain (e.g., robots in warehouses and stores, driverless forklifts and trucks, delivery drones and fully automated planning) is either here or will be by 2025.

However, simply utilizing digital technologies does not equate to creating a digitized, autonomous supply chain — it also needs connected supply chain technologies across planning, procurement, manufacturing and logistics that work beyond the organization's four walls. It's the difference between "doing digital" and "being digital."

We can think about autonomous operations in terms of "lights-out," "hands-free" and "self-driving," where organizations use AI technologies across the end-to-end supply chain to help make predictive and prescriptive decisions. An example is responding to a change in customer demand, seen instantly by the entire value chain (the organizations, its suppliers and their suppliers' suppliers) so they can collectively adjust supply plans and production schedules immediately. Ultimately digital and autonomous technologies will help make people's jobs easier and the supply chain more efficient and optimized.

What comes next?

From the feetatel, we see that 27% of exclusives say the pandemental filed as a Wilei supply chain organization that will fit the new digital and autonomous focused era.

The supply chain of the future will need to be agile, flexible, efficient, resilient and digitally networked for improved visibility. Organizations, therefore, should focus on five priorities for recovery and beyond.

1. Reimagine the strategic architecture of your supply chain

- Rapidly redefine your supply chain strategy and alter global trade flows, considering new trade agreements, country incentives and omnichannel acceleration.
- Reimagine your supply chain operating model what work should get done locally, regionally and globally, including warehouses and manufacturing sites. There are considerable tax implications here, and a new model can also help you prepare for future disruption.

2. Build transparency and resiliency

- Improve disruption response with real-time visibility and monitoring of your end-to-end supply chain, as well as performing scenario planning and simulations.
- Review your supply chain footprint. Do you have alternate sources of supply established? Are you ensuring you do not have vendor or geographic concentration?

3. Extract cash and cost from your supply chain

- Drive a step change in your supply chain cost structure and working capital profile by focusing on SKU
 rationalization, procurement spend reduction, logistics and warehouse optimization, and manufacturing
 productivity.
- Reduce working capital via supply chain segmentation, refreshed inventory planning parameters and changes in payment terms.

4. Create a competitive advantage with sustainability

- The future is a circular economy where there is no waste in your products or manufacturing.
- Explore ways to redesign and engineer new products to achieve this circular economy and monitor third-party risk with supplier sustainability assessments across tiers 1-3.

5. Drive agility and opportunities for growth through a digital supply chain

• Work towards implementing the digital and end-to-end supply chain across planning, procurement, manufacturing and logistics. This can drive efficiencies and also open new revenue streams.

• UREMA1 that a ship a first a far a ship and the fill of the ship and the fill of the ship and the ship and the fill of the ship and t

Many executives are hoping that the COVID-19 pandemic is a once-in-a-lifetime event. However, as the adage goes, "hope is not a strategy." There are ways to stand out and better navigate the storms of the next inevitable disruption. These include reimaging your supply chain strategies for risk and resilience and finding ways to extract cash and invest in digital technologies at speed. It also is important to continually put humans at the center of your efforts and empower them to do extraordinary things. Finally, innovate with customers in mind through a truly sustainable supply chain — one that is designed with circularity and the environment in mind. Following this path, your enterprise will be better prepared to manage whatever crises come next — turning potential disruptions into tremendous opportunities.

Summary

EY research shows that the COVID-19 pandemic accelerated preexisting issues in the supply chain and brought priorities such as visibility, resilience and digitization to the fore. While some sectors were hit hard by disruption, there were some winners, notably life sciences. But across the board, protecting, retraining and reskilling the workforce is a major priority, along with investing to make the autonomous supply chain a reality.

About this article

Sean Harapko

EY Americas Supply Chain Transformation and Global Supply Chain RPA leader

Passionate about friends and family both in and out of work. Husband and father surrounded by girls. Outdoor adventure seeker. Big supporter of the military and military community.



EY | Assurance | Consulting | Strategy and Transactions | Tax

About EY

EY is a global leader in assurance, consulting, strategy and transactions, and tax services. The insights and quality services we deliver help build trust and confidence in the capital markets and in economies the world over. We develop

outstant In Galdre on a chief of the control of the

EY refers to the global organization, and may refer to one or more, of the member firms of Ernst & Young Global Limited, each of which is a separate legal entity. Ernst & Young Global Limited, a UK company limited by guarantee, does not provide services to clients. For more information about our organization, please visit ey.com.

© 2020 EYGM Limited. All Rights Reserved.

EYG/OC/FEA no.

ED MMYY

This material has been prepared for general informational purposes only and is not intended to be relied upon as accounting, tax, or other professional advice. Please refer to your advisors for specific advice.

Source: https://www.statista.com/statistics/1251080/number-of-cruise-passengers-from-north-america/

Number of cruise passengers from North America 2016-2021

Published by Statista Research Department, Jul 18, 2022

The number of cruise passengers sourced from North America declined by roughly 26.4 percent in 2021 over the previous year, following a sharp drop in 2020 due to the coronavirus (COVID-19) pandemic. Overall, passengers from North American countries totaled around 2.2 million in 2021, decreasing from three million in the first year of the health crisis and over 15 million in 2019. Despite the impact of COVID-19, North America was the <u>leading source market in the global cruise industry worldwide</u> in 2021.

Number of cruise passengers sourced from North America from 2016 to 2021 (in 1,000s)

USCA11 Case: 21-12729 Document: 44-2 Date Filed: 10/06/2022 Page: 61 of 95 Additional Information

© Statista 2022

Show source (1)

Source

- → Show sources information
- → Show publisher information
- → Use Ask Statista Research Service

Release date

July 2022

Region

North America

Survey time period

2016 to 2021

Supplementary notes

Figures prior to 2019 were previously published by the source.

(https://flaports.org)







(HTTPS://FLAPORTS.ORG/RESOURCE-

(HTTPS://FLAPORTS.ORG/SEAPORTS/) (HTTPS://FLAPORTS.ORG/ADVOCACY/)

TYPES/DOCUMENTS/)

View Menu



PORTMIAMI • Miami, FL

PortMiami had a record year in FY2021 for containerized cargo. The Port's experienced increases from Latin America, Asia, and Europe. The total TEUs for FY2021 increased 18% to 1,254,062 from 1,066,738 in FY2020.

PortMiami, among the nation's busiest ports, contributes approximately \$43 billion and more than 334,000 jobs annually to Florida's economy. Its sustained performance propels Miami to be recognized as the Cruise Capital of the World and Global Cargo Gateway. After completing more than \$1 billion of capital improvements on the cargo side, including a deep water channel with a depth of -50/52 feet, the acquisition of new super Post-Panamax gantry cranes, upgrades to on-dock intermodal rail providing connectivity to 70% of U.S. population in less than four days, and a fast access tunnel link to the U.S. interstate highway system, the world's largest container shipping alliances have made PortMiami their preferred port solidifying its position as a world class global gateway. To date, the Port has welcomed more than 300 Post-Panamax vessels requiring a -39 ft. draft or deeper that could not have called without the completion of these projects.

For the seventh consecutive year, PortMiami has surpassed the 1 million TEU mark and this past year hit just over the 1.25 million TEU mark.

Goals & Objectives

- Maintain, improve and enhance cruise facilities necessary to accommodate the projected number of cruise passengers and ships
- Maintain, improve and enhance cargo facilities to accommodate the projected cargo volume demands
- Operate with top security measures and ensure compatibility of its facilities and operations with surrounding communities and the natural environment

Current or Planned Investments

 New Cruise Terminals H, AA/AAA, F expansion, Berth 10, shore power at five terminals, and roadway improvements

- New Inland Cargo Ports and Rehabilitated Bulkheads/Berths
- Cargo Container Yard Infrastructure Improvements, including infrastructure for eRTGs,
 Post Panamx gantry cranes, and state-of-the-art cargo gate facilities

Accomplishments

- Consistent cargo growth reflecting over 1 million TEUs for over 5 years in a row
- Cruise growth increase to a record 6.79 million passengers in FY2019 along with new contracts for continued growth
- Continuous safe and secure operations in a sustainable environment

Hinterland

For east-west trade the hinterland extends from the south Florida counties of Miami-Dade, Broward, Monroe and Palm Beach throughout the state. For north-south trade it includes all of Florida and extends into the Southeast, Northeast and Midwest of the United States.

Trade Partners



Mission

PortMiami's mission is to operate and further develop the world's leading cruise port and the largest container port in the State of Florida; to maximize its assets and strengthen its advantage for future growth; promote international trade and commerce as a vital link between North and South America and a growing center for global trade; support sustainability and operate in an environmentally responsible manner.

Governing Body:

Board of County Commissioners, Miami-Dade County

Address:

Dante B. Fascell Port of Miami, 1015 North America Way, 2nd Floor, Miami, Florida 33132 Miami, FL 33132

Phone:

(305) 347-4800

Email:

portofmiami@miamidade.gov (mailto:portofmiami@miamidade.gov)

VISIT WEBSITE (HTTPS://WWW.MIAMIDADE.GOV/PORTMIAMI/HOME.ASP)



RELATED LINKS

- <u>Miami-Dade County Mayor Daniella Levine Cava announces commitment with</u> <u>Carnival Cruise Line for shore power pilot at PortMiami</u>
- <u>(https://flaports.org/miami-dade-county-mayor-daniella-levine-cava-announces-commitment-with-carnival-cruise-line-for-shore-power-pilot-at-portmiami/)</u>
- <u>Carnival Horizon back at PortMiami (https://flaports.org/carnival-horizon-back-at-portmiami/)</u>
- Cruise Capital of the World thanks Senators Rick Scott and Marco Rubio for introducing Set Sail Safely Act (https://flaports.org/cruise-capital-of-the-world-thanks-senators-rick-scott-and-marco-rubio-for-introducing-set-sail-safely-act/)
- MSC Cruises celebrates "float out" of its new MSC Seashore, coming to
 PortMiami November 2021 (https://flaports.org/msc-cruises-celebrates-float-out-of-its-new-msc-seashore-coming-to-portmiami-november-2021/)
- <u>Carnival Cruise Line to grow at PortMiami (https://flaports.org/carnival-cruise-line-to-grow-at-portmiami/)</u>

- Six Florida ports awarded federal funds for security projects
- (https://flaports.org/six-florida-ports-awarded-federal-funds-for-security-projects/)
- PortMiami keeps goods moving from ship to shelf with new cargo handling
 equipment (https://flaports.org/portmiami-keeps-goods-moving-from-ship-to-shelf-with-new-cargo-handling-equipment/)
- PortMiami Growing at Full Speed (https://flaports.org/portmiami-growing-at-full-speed/)
- PortMiami adds new Mediterranean cargo service (https://flaports.org/portmiami-adds-new-mediterranean-cargo-service/)
- <u>U.S. Army Corps of Engineers Releases 2019 Work Plan</u>
 <u>(https://flaports.org/advocacy/u-s-army-corps-of-engineers-releases-2019-work-plan/)</u>

SEAPORTS

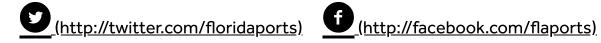
- Port Canaveral (https://flaports.org/ports/port-canaveral/)
- Port Everglades (https://flaports.org/ports/port-everglades/)
- Port of Fernandina (https://flaports.org/ports/port-of-fernandina/)
- Port of Fort Pierce (https://flaports.org/ports/port-of-fort-pierce/)
- JAXPORT (https://flaports.org/ports/jaxport/)

- Port of Key West (https://flaports.org/ports/port-of-key-west/)
- SeaPort Manatee (https://flaports.org/ports/seaport-manatee/)
- PortMiami (https://flaports.org/ports/portmiami/)
- Port of Palm Beach (https://flaports.org/ports/port-of-palm-beach/)
- Port Panama City (https://flaports.org/ports/port-panama-city/)
- Port of Pensacola (https://flaports.org/ports/port-of-pensacola/)
- Port of Port St. Joe (https://flaports.org/ports/port-of-port-st-joe/)
- Port St. Pete (https://flaports.org/ports/port-of-st-petersburg/)
- Port Tampa Bay (https://flaports.org/ports/port-tampa-bay/)

Florida Ports Council

502 East Jefferson Street Tallahassee, Florida 32301

Phone: (850) 222-8028 **Fax:** (850) 222-7552







© Copyright 2022 Florida Ports Council. All Rights Reserved.

(https://flaports.org)







(HTTPS://FLAPORTS.ORG/RESOURCE-

(HTTPS://FLAPORTS.ORG/SEAPORTS/) (HTTPS://FLAPORTS.ORG/ADVOCACY/)

TYPES/DOCUMENTS/)

View Menu



PORT CANAVERAL Cape Canaveral, FL

Port Canaveral is a world-class deep-water seaport for global trade. For nearly seven decades, the Port has served as a critical gateway connecting commerce and consumers throughout Florida and the southeastern United States. Today, the Port continues to play a vital and historic role in supporting U.S. military operations, government, military and commercial space exploration and commerce.

Port Canaveral has a significant position and responsibility in building and sustaining a strong economy on Florida's Space Coast and the Central Florida region – as it is the 10th largest consumer market in the U.S. with economic growth well above the national average. The Port and its Foreign Trade Zone #136 serve as a unique quadri-modal transportation hub: linking sea, land, air and space with the benefits of a deep-water seaport that includes easy and efficient highway access; unrestricted airdraft; -43 deep- water sea access; and, uncongested multipurpose berthing.

Port Canaveral is perhaps best known as the second busiest cruise port in the world, hosting some of the largest cruise vessels from the largest cruise brands in the world with millions of multi-day passenger embarkations annually.

The Port currently has a total of seven cruise terminals with several recently undergoing major renovations to further support industry growth.

Prior to the onset of the global COVID pandemic in March 2020 and the shutdown of cruising in the United States, Port Canaveral was hosting nearly 5 million multi- day revenue cruise passengers annually. In FY 2020 that number dropped to 2,261,431, and in FY 2021 it was 233,216. However, in FY 2022 the number of homeported cruise vessels at Port Canaveral grows to 11 – the highest number of cruise ships in the Port's history — and the Port is anticipating passenger levels to approach or potentially exceed pre-pandemic levels.

Named "World's Best Cruise Port" by Global Traveler Magazine in 2019, and "Best Cruise Port in the U.S." by Cruise Hive in 2019 and 2021, Port Canaveral is the first LNG cruise port in North and South America.

Carnival Cruise Line's Mardi Gras – a 180,000-ton cruise ship powered by cleaner-burning LNG, arrived in June 2021 at the Port's brand new 188,000 sq. ft. Cruise Terminal 3 – the Mardi Gras's new home – and began sailing 7-day Eastern and Western Caribbean itineraries from Port Canaveral on July 31, 2021. The \$163 million terminal, berth works and adjacent 1,800 vehicle parking garage was the largest capital project in the Port's 68-year history.

In FY 2021, to support the arrival of LNG powered vessels, Port Canaveral commissioned into service a high-tech fireboat designed and purpose-built to provide enhanced marine and LNG firefighting and rescue capabilities. The \$4.8 million "Canaveral Fireboat 2" is a 65-foot Marine Firefighting Rescue Vessel equipped with conventional and dry-chemical firefighting apparatus to ensure the safety of the Port's growing maritime operations and expanding space enterprises in the region.

In FY 2019, Port Canaveral hosted nearly 4.6 million revenue cruise passengers through its state-of-the-art terminals and 6 million tons of cargo, including dry and liquid bulk, breakbulk, project, and containerized. In FY 2021, following an 18-month suspension of cruising due to the global COVID pandemic, cruising is gradually resuming from Port Canaveral while cargo operations expanded, continuing a growth pattern which began in FY 2020.

Although approximately 75-percent of the Port's total revenue is derived from its cruise business, the Port has an increasingly diversified cargo portfolio and growing needs to support the region's commercial space operations.

The Port is investing in increasing its operational capabilities and capacity to meet the needs of today's larger more sophisticated vessels; add value to the Port's capabilities; and, to maintain its competitive position for handling current and future business demands.

The Port's five-year capital improvement program was paused in FY 2020 and FY 2021, but is back on track for FY 2022 encompassing harbor and landside infrastructure improvements, such as renovating cruise and cargo terminal facilities, as well as building and refurbishing multi- purpose deep-water berths to keep pace with demands and promote economic prosperity for the region.

Goals & Objectives

- Diversify Port Canaveral's business portfolio with cargo terminal expansion and uplands development projects to accommodate more bulk and breakbulk cargo, energy products storage and distribution (transportation fuels and LNG).
- Increase cargo handling capabilities and add capacity for more flexibility to accommodate diverse commodities and increased heavy lift and project cargo for expanding commercial space operations.

• Improve berth capacities and capabilities to accommodate increasing vessel size and tonnage of cargo and cruise ships.

Current or Planned Investments

- Renovating/rebuilding North Cargo Berths 3 and 4.
- Stormwater improvements and utilities relocation to improve infrastructure resiliency, and expand land utilization and suitability of approximately 34 acres for uplands development.
- Acquiring second mobile harbor crane to substantially increase the Port's cargo handling capabilities.
- Relocating and/or improving access roadways and installing new signaling to improve traffic access /egress and improve public safety and security.
- Cruise terminal expansion and berth improvements to increase flexibility to accommodate larger cruise vessels.

Accomplishments

- \$110 million in total revenue for 2019 (highest in Port history)
- Completion of newly-built Cruise Terminal 3 complex in June 2020 to homeport Carnival Cruise Line's Mardi Gras – the largest and newest class of ship and the first LNG powered cruise ship in North or South America..
- Carnival's Mardi Gras arrived in June 2021 and began revenue sailings on July 31, 2021.

Hinterland

Port Canaveral's hinterland includes the Central Florida region paralleling the I-4 corridor and the Central Florida I-95 corridor.

Cargo: Central and North Florida counties of Brevard, Polk, Indian River, Orange, Osceola, Seminole and Volusia.

Cruise: The U.S., Europe, the Bahamas and the Caribbean, Mexico, and Central and South America.

Trade Partners



Mission

Serve the district and region by facilitating waterborne commerce, creating employment, accommodating port-related business and industry, and otherwise positively impact the economic growth of the district.

Governing Body:

Canaveral Port Authority (Canaveral Port District)

Address:

445 Challenger Road, Suite 301 Cape Canaveral, FL 32920

Phone:

(321) 783-7831

VISIT WEBSITE (HTTP://WWW.PORTCANAVERAL.COM)



RELATED LINKS

- Florida Ports Council Bolsters Professional Staff (https://flaports.org/floridaports-council-bolsters-professional-staff/)
- Rep. Jay Trumbull to Keynote Annual Meeting (https://flaports.org/rep-jay-trumbull-to-keynote-annual-meeting/)
- <u>Debate Over Cruise Vaccination Requirements Continues</u>
 (<u>https://flaports.org/2021-08-16-debate-over-cruise-vaccination-requirements-continues/</u>)

- Florida's Seaports Continue #NavigatingBeyondThePandemic
- (https://flaports.org/floridas-seaports-continuenavigatingbeyondthepandemic/)
- <u>Tropical Shipping is Hiring (https://flaports.org/tropical-shipping-is-hiring/)</u>
- Port Tampa Bay's Annual Fishing Tournament Returns in November
 (https://flaports.org/port-tampa-bays-annual-fishing-tournament-returns-in-november/)
- Port Executive Director Celebrates 13 Years (https://flaports.org/portexecutive-director-celebrates-13-years/)
- Port of Palm Beach Plans to Boost Its Intermodal Rail Capacity and Expand its
 Megayacht Facility (https://flaports.org/port-of-palm-beach-plans-to-boost-its-intermodal-rail-capacity-and-expand-its-megayacht-facility/)
- <u>Eastern Shipbuilding Opens Facility at Port of Port St. Joe</u>
 <u>(https://flaports.org/eastern-shipbuilding-opens-facility-at-port-of-port-st-joe/)</u>
- <u>Fireboat 2 Christened Into Service at Canaveral Dockside Ceremony</u>
 <u>(https://flaports.org/fireboat-2-christened-into-service-at-canaveral-dockside-ceremony/)</u>

SEAPORTS

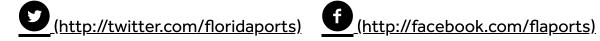
- <u>Port Canaveral (https://flaports.org/ports/port-canaveral/)</u>
- Port Everglades (https://flaports.org/ports/port-everglades/)

- Port of Fernandina (https://flaports.org/ports/port-of-fernandina/) • Port of Fort Pierce (https://flaports.org/ports/port-of-fort-pierce/) JAXPORT (https://flaports.org/ports/jaxport/) Port of Key West (https://flaports.org/ports/port-of-key-west/) <u>SeaPort Manatee (https://flaports.org/ports/seaport-manatee/)</u> PortMiami (https://flaports.org/ports/portmiami/) Port of Palm Beach (https://flaports.org/ports/port-of-palm-beach/) Port Panama City (https://flaports.org/ports/port-panama-city/) • Port of Pensacola (https://flaports.org/ports/port-of-pensacola/) Port of Port St. Joe (https://flaports.org/ports/port-of-port-st-joe/) Port St. Pete (https://flaports.org/ports/port-of-st-petersburg/)
 - Port Tampa Bay (https://flaports.org/ports/port-tampa-bay/)

Florida Ports Council

502 East Jefferson Street Tallahassee, Florida 32301

Phone: (850) 222-8028 Fax: (850) 222-7552





(https://www.linkedin.com/company/the-florida-ports-council)

© Copyright 2022 Florida Ports Council. All Rights Reserved.

(https://flaports.org)







(HTTPS://FLAPORTS.ORG/RESOURCE-

(HTTPS://FLAPORTS.ORG/SEAPORTS/) (HTTPS://FLAPORTS.ORG/ADVOCACY/)

TYPES/DOCUMENTS/)

View Menu



PORT EVERGLADES • Fort Lauderdale, FL

Business diversity and a strong commitment to customer service distinguishes Port Everglades from most U.S. seaports. With its proximity to the popular Caribbean, Port Everglades is the third busiest cruise homeport in the world. It is a leading container port in Florida and among the most active cargo ports nationally.

Port Everglades is also South Florida's main seaport for receiving energy products, including gasoline and jet fuel. Port customers benefit from direct highway access, an international airport within two miles, state-of-the-art foreign-trade zone warehousing and a 43-acre international and domestic intermodal container transfer facility that makes it possible for cargo shipped to Port Everglades to reach Atlanta and Charlotte by rail within two days and 70 percent of the U.S. population in four days. An epicenter for international trade, the Port is positioned in one of the world's largest consumer regions, including a combined 110 million residents and seasonal visitors within an 80-mile radius.

Port Everglades is the U.S. gateway for trade with Latin America, moving 13 percent of all U.S./Latin American trade. The Port's diversified cargo mix includes containers, refrigerated cargo (4th for imports in the United States), new and used automobiles and trucks, dry bulk, breakbulk, project, RO/RO and liquid bulk. Approximately 38 percent of the transportation fuels consumed in Florida are stored and distributed by companies located within Port Everglades, including jet fuel for four international airports.

In a typical, non-COVID year, Port Everglades hosts nearly 4 million cruise passengers annually sailing Caribbean, South American and Transatlantic itineraries offered by a variety of cruise lines and one daily ferry service. Guests enjoy the Port's proximity to three international airports including the rapidly growing Fort Lauderdale-Hollywood International Airport (FLL) less than two miles away. For pre- and post-cruise stays, Port Everglades is a short drive to sweeping beachfronts, a vibrant art scene, world-class restaurants, craft breweries, entertainment, shopping, casinos, and family-friendly activities — including its namesake, the Florida Everglades.

Always striving to modernize its facilities to maximize productivity, Port Everglades follows an aggressive, comprehensive Master/Vision Plan that is updated every 2-4 years to reanalyze market trends, changes in the cruise, cargo shipping and energy industries, local planning initiatives and evolving technology. This in-depth analysis provides a projective and substantiated market-driven and environmentally sound phased roadmap for guiding cost-feasible capital investments.

A Broward County department, Port Everglades does not rely on local tax dollars for operations. The total value of economic activity related to Port Everglades was nearly \$29 billion is fiscal year 2020. More than 196,000 Florida jobs are impacted by the Port, including 10,389 people who work for companies providing direct services.

Through a comprehensive 20-Year Master/Vision Plan, Port Everglades and its consultant Bermello Ajamil & Partners, Inc. (B&A) have identified 50 infrastructure improvements, budgeted from \$1.6 billion to \$3 billion that will increase the Port's productivity over the next five, 10 and 20 years. More than half of the projects will be started and/or completed within the next five years.

Goals & Objectives

- Complete the Southport Turning Notch Extension and crane rail infrastructure project.
- Develop a shore power program for cruise ships with Florida Power & Light and cruise line partners.
- Complete the U.S. Army Corps of Engineers Port Everglades Navigation Improvement Project.
- Diversify cruise line mix and begin renovations to Cruise Terminal 4 for Disney Cruise Line.

Current or Planned Investments

- Construction is 75 percent completed on the largest infrastructure project in the Port's
 history. The Southport Turning Notch Extension, slated for completion in late 2023, will add
 new cargo berths and Super Post-Panamax container gantry cranes to the Port's main
 containerized cargo area by lengthening the existing turnaround area (turning notch) from
 900 feet to 2,400 feet. Part of the \$471 million project includes installing crane rail
 infrastructure to handle new Super Post-Panamax container gantry cranes and the Port's
 existing cranes.
- Port Everglades commissioned three Super Post- Panamax container gantry cranes in February 2021 at \$13.8 million each to meet demands from current customers and new

services anticipated from the Port's multi-million-dollar expansion program. Three additional Super Post-Panamax container gantry cranes are under construction and anticipated to arrive in late 2024.

- To further enhance ship traffic at Port Everglades, the U.S. Army Corps of Engineers
 (USACE) is advancing a 24-year plan to deepen the Port's navigation channels from 42 feet
 to 48-50 feet and widen narrower sections of the channel for safe vessel passage.
 Construction is anticipated to be completed by 2030.
- In the Port's energy sector, a \$184-million Slip 1 expansion will allow the Port to safely service the petroleum industry with greater capacity, efficiency, sustainability and resiliency. This is a public-private partnership, with the civil infrastructure being constructed by the Port and petroleum transfer infrastructure being installed by private industry partners.

Accomplishments

- Received first three of six low profile super post-Panamax gantry cranes in November 2020, placed into service in late February 2021, and commissioned with a combination live and "virtual" ceremony on March 21, 2021.
- Completed construction on the 1,818-space, state-of-the-art Heron Parking Garage, which serves Cruise Terminals 2 and 4.
- Received a construction "New Start" designation in the U.S. Army Corps of Engineers
 (USACE) FY 2020 Work Plan. The New Start designation funds \$29.1 million to build a new
 facility for the U.S. Coast Guard (USCG) Station in Fort Lauderdale.

Hinterland

Cargo:

Port Everglades is in the heart of one of the world's largest consumer regions, with a constant flow of seasonal visitors and up to 110 million residents plus within a 500-mile radius. The

Florida East Coast Railway's 43-acre intermodal container transfer facility makes it possible for cargo shipped into Port Everglades to reach Atlanta and Charlotte in two days, Memphis and Nashville in three days, and 70 percent of the U.S. population in four days.

Cruise:

The Caribbean, Central America, South America, Panama Canal and Europe.

Trade Partners



Mission

As a premier gateway and powerhouse for international trade, travel and investment, Broward County's Port Everglades leverages its world-class South Florida facilities and innovative leadership to drive the region's economic vitality and provide unparalleled levels of service, safety, environmental stewardship and community engagement.

Governing Body:

Broward County Board of County Commissioners

Address:

1850 Eller Drive Fort Lauderdale, FL 33316

Phone:

(954) 523-3404

Email:

porteverglades@broward.org (mailto:porteverglades@broward.org)

VISIT WEBSITE (HTTP://WWW.PORTEVERGLADES.NET)



RELATED LINKS

- Port Everglades commissions new super-sized cranes (https://flaports.org/porteverglades-commissions-new-super-sized-cranes/)
- <u>CMA CGM selects Port Everglades and FIT for new FLAMINGO EXPRESS service</u>
 <u>(https://flaports.org/cma-cgm-selects-port-everglades-and-fit-for-new-flamingo-express-service/)</u>
- Port Everglades receives "Marine Highway" designation from MARAD
 (https://flaports.org/port-everglades-receives-marine-highway-designation-from-marad/)

- Rehoboth, a small business success story at Port Everglades
- (https://flaports.org/rehoboth-a-small-business-success-story-at-port-everglades/)
- <u>Six Florida ports awarded federal funds for security projects</u>
 <u>(https://flaports.org/six-florida-ports-awarded-federal-funds-for-security-projects/)</u>
- Broward County selects Jonathan Daniels to lead Port Everglades
 (https://flaports.org/county-selects-jonathan-daniels-to-lead-port-everglades/)
- Port Everglades Expansion On Track (https://flaports.org/port-evergladesexpansion-on-track/)
- Port Everglades Welcomes Princess Cruises' Sky Princess
 (https://flaports.org/port-everglades-welcomes-princess-cruises-sky-princess/)
- Port Everglades Upgrades Inventory Warehouse (https://flaports.org/porteverglades-upgrades-inventory-warehouse/)
- Port Everglades Welcomes Carnival Sunrise to Her New Winter Homeport
 (https://flaports.org/port-everglades-welcomes-carnival-sunrise-to-her-new-winter-homeport/)

SEAPORTS

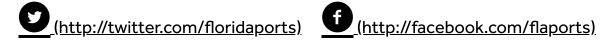
• Port Canaveral (https://flaports.org/ports/port-canaveral/)

- Port Everglades (https://flaports.org/ports/port-everglades/) Port of Fernandina (https://flaports.org/ports/port-of-fernandina/) Port of Fort Pierce (https://flaports.org/ports/port-of-fort-pierce/) JAXPORT (https://flaports.org/ports/jaxport/) Port of Key West (https://flaports.org/ports/port-of-key-west/) SeaPort Manatee (https://flaports.org/ports/seaport-manatee/) PortMiami (https://flaports.org/ports/portmiami/) Port of Palm Beach (https://flaports.org/ports/port-of-palm-beach/) Port Panama City (https://flaports.org/ports/port-panama-city/) Port of Pensacola (https://flaports.org/ports/port-of-pensacola/) Port of Port St. Joe (https://flaports.org/ports/port-of-port-st-joe/) Port St. Pete (https://flaports.org/ports/port-of-st-petersburg/)
 - Port Tampa Bay (https://flaports.org/ports/port-tampa-bay/)

Florida Ports Council

502 East Jefferson Street Tallahassee, Florida 32301

Phone: (850) 222-8028 Fax: (850) 222-7552





(https://www.linkedin.com/company/the-florida-ports-council)

© Copyright 2022 Florida Ports Council. All Rights Reserved.

FDA NEWS RELEASE

FDA Approves First COVID-19 Vaccine

Approval Signifies Key Achievement for Public Health

For Immediate Release:

August 23, 2021

Español (https://www.fda.gov/news-events/press-announcements/la-fda-aprueba-la-primera-vacuna-contra-el-covid-19)

Today, the U.S. Food and Drug Administration approved the first COVID-19 vaccine. The vaccine has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty (koe-mir'-na-tee), for the prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under emergency use authorization (EUA), including for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.

"The FDA's approval of this vaccine is a milestone as we continue to battle the COVID-19 pandemic. While this and other vaccines have met the FDA's rigorous, scientific standards for emergency use authorization, as the first FDA-approved COVID-19 vaccine, the public can be very confident that this vaccine meets the high standards for safety, effectiveness, and manufacturing quality the FDA requires of an approved product," said Acting FDA Commissioner Janet Woodcock, M.D. "While millions of people have already safely received COVID-19 vaccines, we recognize that for some, the FDA approval of a vaccine may now instill additional confidence to get vaccinated. Today's milestone puts us one step closer to altering the course of this pandemic in the U.S."

Since Dec. 11, 2020, the Pfizer-BioNTech COVID-19 Vaccine has been available under EUA in individuals 16 years of age and older, and the authorization was expanded to include those 12 through 15 years of age on May 10, 2021. EUAs can be used by the FDA during public health emergencies to provide access to medical products that may be effective in preventing, diagnosing, or treating a disease, provided that the FDA determines that the known and potential benefits of a product, when used to prevent, diagnose, or treat the disease, outweigh the known and potential risks of the product.

FDA-approved vaccines undergo the agency's standard process for reviewing the quality, safety and effectiveness of medical products. For all vaccines, the FDA evaluates data and information included in the manufacturer's submission of a biologics license application (BLA). A BLA is a

comprehensive document that is submitted to the agency providing very specific requirements. For Comirnaty, the BLA builds on the extensive data and information previously submitted that supported the EUA, such as preclinical and clinical data and information, as well as details of the manufacturing process, vaccine testing results to ensure vaccine quality, and inspections of the sites where the vaccine is made. The agency conducts its own analyses of the information in the BLA to make sure the vaccine is safe and effective and meets the FDA's standards for approval.

Comirnaty contains messenger RNA (mRNA), a kind of genetic material. The mRNA is used by the body to make a mimic of one of the proteins in the virus that causes COVID-19. The result of a person receiving this vaccine is that their immune system will ultimately react defensively to the virus that causes COVID-19. The mRNA in Comirnaty is only present in the body for a short time and is not incorporated into - nor does it alter - an individual's genetic material. Comirnaty has the same formulation as the EUA vaccine and is administered as a series of two doses, three weeks apart.

"Our scientific and medical experts conducted an incredibly thorough and thoughtful evaluation of this vaccine. We evaluated scientific data and information included in hundreds of thousands of pages, conducted our own analyses of Comirnaty's safety and effectiveness, and performed a detailed assessment of the manufacturing processes, including inspections of the manufacturing facilities," said Peter Marks, M.D., Ph.D., director of FDA's Center for Biologics Evaluation and Research. "We have not lost sight that the COVID-19 public health crisis continues in the U.S. and that the public is counting on safe and effective vaccines. The public and medical community can be confident that although we approved this vaccine expeditiously, it was fully in keeping with our existing high standards for vaccines in the U.S."

FDA Evaluation of Safety and Effectiveness Data for Approval for 16 Years of Age and Older

The first <u>EUA (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19)</u>, issued Dec. 11, for the Pfizer-BioNTech COVID-19 Vaccine for individuals 16 years of age and older was <u>based on safety and effectiveness data (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19) from a randomized, controlled, blinded ongoing clinical trial of thousands of individuals.</u>

To support the FDA's approval decision today, the FDA reviewed updated data from the clinical trial which supported the EUA and included a longer duration of follow-up in a larger clinical trial population.

Specifically, in the FDA's review for approval, the agency analyzed effectiveness data from 95 approximately 20,000 vaccine and 20,000 placebo recipients ages 16 and older who did not have evidence of the COVID-19 virus infection within a week of receiving the second dose. The safety of Comirnaty was evaluated in approximately 22,000 people who received the vaccine and 22,000 people who received a placebo 16 years of age and older.

Based on results from the clinical trial, the vaccine was 91% effective in preventing COVID-19 disease.

More than half of the clinical trial participants were followed for safety outcomes for at least four months after the second dose. Overall, approximately 12,000 recipients have been followed for at least 6 months.

The most commonly reported side effects by those clinical trial participants who received Comirnaty were pain, redness and swelling at the injection site, fatigue, headache, muscle or joint pain, chills, and fever. The vaccine is effective in preventing COVID-19 and potentially serious outcomes including hospitalization and death.

Additionally, the FDA conducted a rigorous evaluation of the post-authorization safety surveillance data pertaining to myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine and has determined that the data demonstrate increased risks, particularly within the seven days following the second dose. The observed risk is higher among males under 40 years of age compared to females and older males. The observed risk is highest in males 12 through 17 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. However, some individuals required intensive care support. Information is not yet available about potential long-term health outcomes. The Comirnaty Prescribing Information includes a warning about these risks.

Ongoing Safety Monitoring

The FDA and Centers for Disease Control and Prevention have monitoring systems in place to ensure that any safety concerns continue to be identified and evaluated in a timely manner. In addition, the FDA is requiring the company to conduct postmarketing studies to further assess the risks of myocarditis and pericarditis following vaccination with Comirnaty. These studies will include an evaluation of long-term outcomes among individuals who develop myocarditis following vaccination with Comirnaty. In addition, although not FDA requirements, the company has committed to additional post-marketing safety studies, including conducting a pregnancy registry study to evaluate pregnancy and infant outcomes after receipt of Comirnaty during pregnancy.

The FDA granted this application <u>Priority Review (https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review)</u>. The approval was granted to BioNTech Manufacturing GmbH.

Related Information Document: 44-2 Date Filed: 10/06/2022 Page: 91 of 95

- Comirnaty Prescribing Information (http://www.fda.gov/vaccines-bloodbiologics/comirnaty)
- Cormirnaty and Pfizer-BioNTech COVID-19 Vaccine | FDA (/emergency-preparednessand-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccines)

###

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Inquiries

Media:

FDA Office of Media Affairs (mailto:fdaoma@fda.hhs.gov)

**** 301-796-4540

Consumer:

888-INFO-FDA

More Press Announcements (/news-events/newsroom/press-announcements)

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Takes Key Action by Approving Second COVID-19 Vaccine

For Immediate Release:

January 31, 2022

Español (/news-events/press-announcements/actualizacion-sobre-el-coronavirus-covid-19-la-fda-toma-una-medida-clave-al-aprobar-la-segunda)

Today, the U.S. Food and Drug Administration approved a second COVID-19 vaccine. The vaccine has been known as the Moderna COVID-19 Vaccine; the approved vaccine will be marketed as Spikevax for the prevention of COVID-19 in individuals 18 years of age and older.

Key points:

- Spikevax meets the FDA's rigorous standards for safety, effectiveness and manufacturing quality required for approval.
- Moderna COVID-19 Vaccine has been <u>available under (https://www.fda.gov/news-events/press-announcements/fda-takes-additional-action-fight-against-covid-19-issuing-emergency-use-authorization-second-covid)</u> emergency use authorization (EUA) for individuals 18 years of age and older since Dec. 18, 2020.

"The FDA's approval of Spikevax is a significant step in the fight against the COVID-19 pandemic, marking the second vaccine approved to prevent COVID-19. The public can be assured that Spikevax meets the FDA's high standards for safety, effectiveness and manufacturing quality required of any vaccine approved for use in the United States," said Acting FDA Commissioner Janet Woodcock, M.D. "While hundreds of millions of doses of Moderna COVID-19 Vaccine have been administered to individuals under emergency use authorization, we understand that for some individuals, FDA approval of this vaccine may instill additional confidence in making the decision to get vaccinated."

Spikevax has the same formulation as the EUA Moderna COVID-19 Vaccine and is administered as a primary series of two doses, one month apart. Spikevax can be used interchangeably with the EUA Moderna COVID-19 Vaccine to provide the COVID-19 vaccination series. Moderna COVID-19 Vaccine remains available under EUA as a two-dose primary series for individuals 18 years of age and older, as a third primary series dose for individuals 18 years of age and older who have been determined to have certain kinds of immunocompromise, and as a single booster

dose for individuals 18 years of age and older at least five Filed this after completing a primary series of the vaccine. It is also authorized for use as a heterologous (or "mix and match") single booster dose for individuals 18 years of age and older following completion of primary vaccination with a different available COVID-19 vaccine.

"The FDA's medical and scientific experts conducted a thorough evaluation of the scientific data and information included in the application pertaining to the safety, effectiveness, and manufacturing quality of Spikevax. This includes the agency's independent verification of analyses submitted by the company, our own analyses of the data, along with a detailed assessment of the manufacturing processes, test methods and manufacturing facilities," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "Safe and effective vaccines are our best defense against the COVID-19 pandemic, including currently circulating variants. The public can be assured that this vaccine was approved in keeping with the FDA's rigorous scientific standards."

FDA Evaluation of Effectiveness Data for Approval for Individuals 18 Years of Age and Older

The Spikevax biologics license application (BLA) builds upon the data and information that supported the EUA, such as preclinical and clinical data, as well as details of the manufacturing process and the sites where the vaccine is made. The FDA evaluates and conducts its own analyses of the data to determine whether the safety and effectiveness of the vaccine has been demonstrated and meets the standard for approval, and whether the manufacturing and facility information assure vaccine quality and consistency.

The approval of Spikevax is based on the FDA's evaluation and analysis of follow-up safety and effectiveness data from the ongoing randomized, placebo-controlled, blinded clinical trial that supported the December 2020 EUA for the Moderna COVID-19 Vaccine and information from post EUA experience to further inform safety and effectiveness.

The updated analyses to determine effectiveness of Spikevax included 14,287 vaccine recipients and 14,164 placebo recipients 18 years of age and older who did not have evidence of SARS-CoV-2 infection prior to receiving the first dose. The data used for the analyses were accrued before the Omicron variant emerged. These data demonstrated that Spikevax was 93% effective in preventing COVID-19, with 55 cases of COVID-19 occurring in the vaccine group and 744 COVID-19 cases in the placebo group. The vaccine was also 98% effective in preventing severe disease.

FDA Evaluation of Safety Data for Approval for Individuals 18 Years of Age and Older

The FDA's safety analysis of Spikevax included approximately 15,184 vaccine recipients and 15,162 placebo recipients 18 years of age and older, more than half of these participants were followed for safety outcomes for at least four months after the second dose. Approximately 7,500 participants originally assigned to receive Spikevax in the blinded phase of the clinical trial completed safety follow-up for at least 6 months after the second dose.

The most commonly reported side effects by clinical trial participants were pain, redness and swelling at the injection site, fatigue, headache, muscle or joint pain, chills, nausea/vomiting, swollen lymph nodes under the arm and fever.

Additionally, the FDA conducted a rigorous evaluation of the post-authorization safety surveillance data pertaining to myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of tissue surrounding the heart) following vaccination with the Moderna COVID-19 Vaccine and has determined that the data demonstrate increased risks particularly within seven days following the second dose, with the observed risk highest in males 18 through 24 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. However, some individuals required intensive care support. Information is not yet available about potential long-term health outcomes. The Spikevax Prescribing Information (https://www.fda.gov/media/155675/download) includes a warning about these risks.

The FDA conducted its own benefit-risk assessment using modeling to predict how many symptomatic COVID-19 cases, hospitalizations, intensive care unit (ICU) admissions and deaths from COVID-19 the vaccine in individuals 18 years of age and older would prevent versus the number of potential myocarditis/pericarditis cases, hospitalizations, ICU admissions and deaths that might be associated with the vaccine. FDA has determined that the benefits of the vaccine outweigh the risk of myocarditis and pericarditis in individuals 18 years of age and older.

The FDA is requiring the company to conduct postmarketing studies to further assess the risks of myocarditis and pericarditis following vaccination with Spikevax. These studies will include an evaluation of long-term outcomes among individuals who develop myocarditis following vaccination with Spikevax. In addition, although not FDA requirements, the company has committed to conducting additional post-marketing safety studies, including conducting a pregnancy registry study to evaluate pregnancy and infant outcomes after receipt of Spikevax during pregnancy.

The FDA granted this application <u>Priority Review (https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review)</u>. The approval was granted to ModernaTX, Inc.

Related Information

- -USpikevax COVID-13729cine (https://www.fda.gote/Filed:n10/b6/2023iologics/spikevax)
- <u>Moderna COVID-19 Vaccine (https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine)</u>
- <u>COVID-19 Vaccines (https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines)</u>

###

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Inquiries

Media:

FDA Office of Media Affairs (mailto:fdaoma@fda.hhs.gov)

**** 301-796-4540

Consumer:

♥ 888-INFO-FDA

More Press Announcements (/news-events/newsroom/press-announcements)